EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	0	lamotrigene same particle adj size	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/24 07:32
S2	7	lamotrigene	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/04/04 15:24
S3	23310	particles same specific adj surface adj area	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/23 17:04
S4	163	S3 and pharmaceutical adj composition	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/23 17:51
S5	0	lamotrigene same Teva adj Pharmaceutical?	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/23 17:54
S6	0	lamotrigene same Teva	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/23 17:52
S7	1	("3090693").PN.	US-PGPUB; USPAT	OR	OFF	2006/08/23 18:21
S8	1	("5861179").PN.	US-PGPUB; USPAT	OR	OFF	2006/08/23 18:21
S9	0	bet near particle adj size near surface adj area	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/24 07:33
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S11	3	S10 and BET adj measure?	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/24 12:25
S12	3	(("4847249") or ("5942510") or ("5861179")).PN.	US-PGPUB; USPAT	OR	OFF	2006/08/24 12:31
S13	1	("4602017").PN.	US-PGPUB; USPAT	OR	OFF	2006/08/24 15:06

EAST Search History

S14	1	("0021121").PN.	US-PGPUB; USPAT	OR	OFF	2006/08/24 15:08
S15	1	("4486354").PN.	US-PGPUB; USPAT	OR	OFF	2006/08/24 15:08
S16	7	(("4486354") or ("5643591") or ("4602017") or ("6639072") or ("5925755") or ("5942510") or ("5861179")).PN.	US-PGPUB; USPAT	OR	OFF	2006/08/25 09:16
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S18	3731	S17 and @ad<="20030801"	US-PGPUB; USPAT; USOCR	OR	ON	2007/04/04 16:07
S19	160	((JUDITH) near2 (ARONHIME)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2007/04/04 15:49
S20	5	((GUY) near2 (SAMBURSKI)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2007/04/04 15:20
S21	88	((JUDITH) near2 (ARONHIME)).INV.	EPO; JPO; DERWENT	OR	ON	2007/04/04 15:21
S22	6	((GUY) near2 (SAMBURSKI)).INV.	EPO; JPO; DERWENT	OR	ON	2007/04/04 15:21
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S24	509	S23 and @ad<="20030801"	US-PGPUB; USPAT; USOCR	OR	ON	2007/04/04 15:22
S25	0	"3,5-diamino-6-(2, 3-dichlorophenyl)-1,2,4-triazine"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/04/04 15:44
S26	8	"LAMOTRIGENE"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/04/04 15:29
S27	0	"6-(2,3-dichlorophenyl)-1,2, 4-triazine-3,5-diamine"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/04/04 15:44
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EAST Search History

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S30	1	("6861426").PN.	US-PGPUB; USPAT	OR	OFF	2007/04/04 16:06
S31	1	lamotrigene.clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/04/04 16:07
S32	2	lamotrigene.ti.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/04/04 16:07
S33	65	lamotrigine.ti.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/04/04 16:07
S34	202	lamotrigine.clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/04/04 16:07
S35	12	S33 and @ad<="20030801"	US-PGPUB; USPAT; USOCR	OR	ON	2007/04/04 16:14
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S37	0	("5861179").URPN.	USPAT	OR	ON	2007/04/04 16:09
S38	1	("5912345").URPN.	USPAT	OR	ON	2007/04/04 16:10
S39	38	S36 and particl??	US-PGPUB; USPAT; USOCR	OR	ON	2007/04/04 16:15

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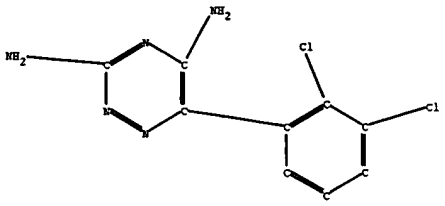
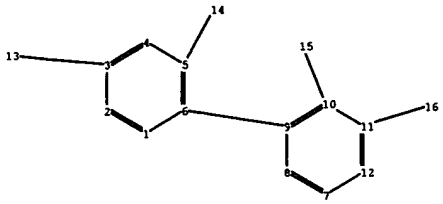
STN
lwl
4/4/07





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13 14 15 16
ring nodes :
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ring bonds :
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exact bonds :
6-9 10-15 11-16
normalized bonds :
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Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS

10/511987 LAMOTRIGINE reg no-text search USPGPUB search

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=> d his

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     FILE 'REGISTRY' ENTERED AT 16:55:37 ON 04 APR 2007
L1              STRUCTURE UPLOADED
L2            3 S L1 SSS SAM
L3          128 S L1 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 16:56:47 ON 04 APR 2007
L4           25 S L3/P
                E US20050238724/PN,PRN,AN
L5            0 S E3/RN
L6            1 S E3

     FILE 'REGISTRY' ENTERED AT 16:58:38 ON 04 APR 2007
L7            0 S L6

     FILE 'HCAPLUS' ENTERED AT 17:00:04 ON 04 APR 2007
                E LAMOTRIGINE+ALL/CT
                S LAMOTRIGINE/CN

     FILE 'REGISTRY' ENTERED AT 17:00:26 ON 04 APR 2007
L8            1 S LAMOTRIGINE/CN

     FILE 'HCAPLUS' ENTERED AT 17:00:27 ON 04 APR 2007
L9         1265 S L8
L10          27 S "3,5-DIAMINO-6-(2,3-DICHLOROPHENYL)-1,2,4-TRIAZINE"

     FILE 'REGISTRY' ENTERED AT 17:02:26 ON 04 APR 2007
L11           1 S 84057-84-1/RN

     FILE 'HCAPLUS' ENTERED AT 17:02:48 ON 04 APR 2007
L12        1265 S L11
L13      111187 S L10 OR L12  AND PARTICLE OR GRANULE
L14           0 S L12 (N) PARTICLE
L15           0 S L12 (W) PARTICLE
L16          46 S L12 AND CNS
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L1 STRUCTURE UPLOADED

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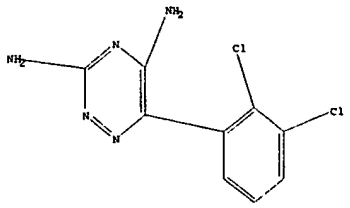

Structure attributes must be viewed using STN Express query preparation.

=> s l1 sss sam
SAMPLE SEARCH INITIATED 16:56:05 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 9 TO ITERATE

100.0% PROCESSED 9 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 9 TO 360
PROJECTED ANSWERS: 3 TO 163

L2 3 SEA SSS SAM L1

=> d l2 1-3 ibib abs
'IBIB' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'ABS' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual fields or predefined formats. The predefined substance formats are: (RN = CAS Registry Number)

REG - RN
SAM - Index Name, MF, and structure - no RN
FIDE - All substance data, except sequence data
IDE - FIDE, but only 50 names
SQIDE - IDE, plus sequence data
SQIDE3 - Same as SQIDE, but 3-letter amino acid codes are used
SQD - Protein sequence data, includes RN

SQD3 - Same as SQD, but 3-letter amino acid codes are used
SQN - Protein sequence name information, includes RN

CALC - Table of calculated properties
EPROP - Table of experimental properties
PROP - EPROP and CALC

Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ABS -- Abstract
APPS -- Application and Priority Information
BIB -- CA Accession Number, plus Bibliographic Data
CAN -- CA Accession Number
CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
IND -- Index Data
IPC -- International Patent Classification
PATS -- PI, SO
STD -- BIB, IPC, and NCL

IABS -- ABS, indented, with text labels
IBIB -- BIB, indented, with text labels
ISTD -- STD format, indented

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available.
The MAX format is the same as ALL.
The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

For additional information, please consult the following help messages:

HELP DFIELDS -- To see a complete list of individual display fields.
HELP FORMATS -- To see detailed descriptions of the predefined formats.
ENTER DISPLAY FORMAT (IDE):ide

L2 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2007 ACS on STN
RN 885316-75-6 REGISTRY
ED Entered STN: 23 May 2006
CN Butanoic acid, 4-[[2-[[4-[[3,4-dichloro-5-(3,5-diamino-1,2,4-triazin-6-yl)phenyl]amino]-1,4-dioxobutyl]amino]ethyl]amino]-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)
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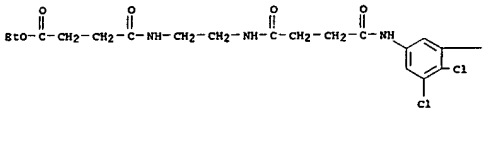
SR CA
LC STN Files: CA, CAPLUS

PAGE 1-A



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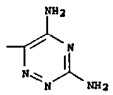

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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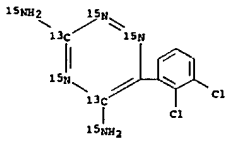
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2007 ACS on STN
RN 478189-71-8 REGISTRY
ED Entered STN: 06 Jan 2003
CN 1,2,4-Triazine-3,5-diamine-3,5-13C2-N,N',1,2,4-15N5, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)
MF C9 H7 Cl2 N5
SR CA
LC STN Files: CA, CAPLUS, CASREACT



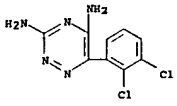
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2007 ACS on STN
RN 454695-04-6 REGISTRY
ED Entered STN: 25 Sep 2002
CN Formamide, N,N-dimethyl-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-

triazine-3,5-diamine (3:2) (9CI) (CA INDEX NAME)
MF C9 H7 Cl2 N5 . 3/2 C3 H7 N O
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 68-12-2
CMF C3 H7 N O

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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100.0% PROCESSED 212 ITERATIONS 128 ANSWERS
SEARCH TIME: 00.00.01

L3 128 SEA SSS FUL L1

=> fil hcaplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	178.40	178.61

FILE 'HCAPLUS' ENTERED AT 16:56:47 ON 04 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 4 Apr 2007 VOL 146 ISS 15
FILE LAST UPDATED: 3 Apr 2007 (20070403/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his

(FILE 'HOME' ENTERED AT 16:55:13 ON 04 APR 2007)

FILE 'REGISTRY' ENTERED AT 16:55:37 ON 04 APR 2007
L1 STRUCTURE UPLOADED
L2 3 S L1 SSS SAM
L3 128 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 16:56:47 ON 04 APR 2007

=> s l3/p
L4 25 L3/P

=> d l4 1-25 ibib abs

L4 ANSWER 1 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:411970 HCAPLUS
DOCUMENT NUMBER: 144:425648
TITLE: Lamotrigine analogs for production of anti-lamotrigine antibodies and use as immunoassay reagents
INVENTOR(S): Ouyang, Anlong; Arabshahi, Lili; Roberts, Mark; Wall, Melissa
PATENT ASSIGNEE(S): Seradyn, Inc., USA
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006047372	A2	20060504	WO 2005-US38100	20051021
WO 2006047372	A3	20060727		
WO 2006047372	A9	20061005		

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2006115865	A1	20060601	US 2005-254650	20051020
PRIORITY APPLN. INFO.:			US 2004-621764P	P 20041025
			US 2005-254650	A 20051020

OTHER SOURCE(S): MARPAT 144:425648
AB The invention discloses lamotrigine analogs that have substituents at the triazine 3-position and on the benzene 4-position and 5-position. The lamotrigine analogs can include immunogenic moieties that can be used to prepare anti-lamotrigine antibodies, or antigenic moieties that can be used in immunodiagnostic assays for lamotrigine. Also, the lamotrigine analog can include tracer moieties for detecting the presence or amount of the analog during an immunodiagnostic assay. Addnl., the lamotrigine analogs can be used in immunodiagnostic assays to compete with lamotrigine for binding with anti-lamotrigine antibodies. Lamotrigine analog preparation is described.

L4 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:411913 HCAPLUS
DOCUMENT NUMBER: 144:425647
TITLE: Immunoassays for lamotrigine
INVENTOR(S): Ouyang, Anlong; Arabshahi, Lili; Roberts, Mark; Wall, Melissa
PATENT ASSIGNEE(S): Seradyn, Inc., USA
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006047451	A2	20060504	WO 2005-US38258	20051021

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2006172356	A1	20060803	US 2005-254637	20051020
PRIORITY APPLN. INFO.:			US 2004-621764P	P 20041025
			US 2005-254637	A 20051020

OTHER SOURCE(S): MARPAT 144:425647
AB Generally, the present invention relates to lamotrigine analogs that have substituents at the triazine 3-position and on the benzene 4-position and 5-position. The lamotrigine analogs can include immunogenic moieties that can be used to prepare anti-lamotrigine antibodies, or antigenic moieties that can be used in immunodiagnostic assays for lamotrigine. Also, the lamotrigine analog can include tracer moieties for detecting the presence

or amount of the analog during an immunodiagnostic assay. Addnl., the lamotrigine analogs can be used in immunodiagnostic assays to compete with lamotrigine for binding with anti-lamotrigine antibodies.

L4 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1010006 HCAPLUS
DOCUMENT NUMBER: 144:312050
TITLE: A new approach to the synthesis of lamotrigine and other 3,5-diamino-1,2,4-triazine derivatives
AUTHOR(S): Ulomskii, E. N.; Shestakova, T. S.; Deev, S. L.; Rusinov, V. L.; Chupakhin, O. N.
CORPORATE SOURCE: Ural State Technical University, Yekaterinburg, 620002, Russia
SOURCE: Russian Chemical Bulletin (2005), 54(3), 726-732
CODEN: RCBUBY; ISSN: 1066-5285
PUBLISHER: Springer Science+Business Media, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new in principle method for the synthesis of 6-aryl(hetaryl)-3,5-diamino-1,2,4-triazines by decomposition of pre-synthesized tetrazolo[1,5-b][1,2,4]triazines was developed. The advantages of this method over traditional methods were demonstrated using the synthesis of a modern antiepileptic preparation lamotrigine, as an example. The crystal structure of 6-phenyltetrazolo[1,5-b][1,2,4]triazin-7-amine is presented [monoclinic, space group P21/c, a 10.935(2), b 6.7330(10), c 13.279(3) Å, β 93.20(3)°, V 976.1(3) Å3, Z 4].
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:421792 HCAPLUS
DOCUMENT NUMBER: 142:430313
TITLE: Process for preparation of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (Lamotrigine) via reaction of 2,3-dichlorobenzoyl chloride with cuprous cyanide and then with aminoguanidine bicarbonate followed by cyclization.
INVENTOR(S): Vyas, Sharad Kumar
PATENT ASSIGNEE(S): Torrent Pharmaceuticals Ltd., India
SOURCE: Indian, 12 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 183150	A1	19990925	IN 1998-CA2171	19981214
CA 2334937	A1	20000622	CA 1999-2334937	19991207
CA 2334937	C	20040921		
WO 2000035888	A1	20000622	WO 1999-IB1955	19991207

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CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2000012924	A	20000703	AU 2000-12924	19991207
EP 1140872	A1	20011010	EP 1999-956293	19991207
EP 1140872	B1	20030917		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

AT 250041	T	20031015	AT 1999-956293	19991207
RU 2231526	C2	20040627	RU 2001-115698	19991207
US 6111101	A	20000829	US 1999-456501	19991208
			IN 1998-CA2171	A 19981214
PRIORITY APPLN. INFO.:			WO 1999-IB1955	W 19991207

OTHER SOURCE(S): CASREACT 142:430313
AB Lamotrigine was prepared by reaction of 2,3-dichlorobenzoyl chloride with CuCN (1:1-2 molar ratio) in MeCN and a cosolvent to produce dichlorobenzoyl cyanide, reaction of the latter with aminoguanidine bicarbonate to produce the cyanoimine intermediate 2-[cyano(2,3-dichlorophenyl)methylene]hydrazinecarboximidamide, and cyclization of this in the presence of aqueous KOH at 80°-reflux.

L4 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:421470 HCAPLUS
DOCUMENT NUMBER: 141:7119
TITLE: Preparation of crystalline lamotrigine and its monohydrate
INVENTOR(S): Manjunatha, Sulur G.; Kulkarni, Ashok Krishna; Kishore, Charugundla; Bokka, Ravisankar
PATENT ASSIGNEE(S): Jubilant Organosys Limited, India
SOURCE: Brit. UK Pat. Appl., 25 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

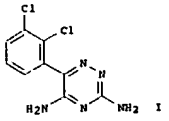
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2395483	A	20040526	GB 2003-15608	20030703
WO 2005003104	A2	20050113	WO 2004-IN186	20040628
WO 2005003104	A3	20050922		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SO, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:			GB 2003-15608	A 20030703

OTHER SOURCE(S): CASREACT 141:7119
GI



I

AB The invention relates to crystalline lamotrigine (3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine) (I) monohydrate and anhydrous lamotrigine. An improved process for manufacturing these products comprises reacting 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in aqueous mineral acid, optionally together with a water miscible organic solvent, at 30-80° to produce the 2-(2,3-dichlorophenyl)-2-(guanidinylimino)acetonitrile (Schiff base) (II). The Schiff base II is further cyclized in aqueous organic solvent, e.g. alc. to produce pure lamotrigine of a pharmaceutically acceptable quality which on further drying at 45-50° under vacuum yields lamotrigine monohydrate, and/or on further drying at 100-110° yields anhydrous lamotrigine. The lamotrigine monohydrate or anhydrous lamotrigine thereby produced may then be brought into association with a pharmaceutically acceptable carrier for administration to a patient in need thereof.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

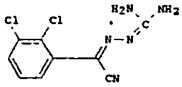
L4 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:390214 HCAPLUS
DOCUMENT NUMBER: 140:391299
TITLE: Process for preparing 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile and a process for its cyclization into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine
INVENTOR(S): Dalmases Barjoan, Pere; Bessa Bellmunt, Jordi
PATENT ASSIGNEE(S): Laboratorios Vita, S.A., Spain
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

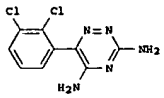
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039767	A1	20040513	WO 2003-IB4763	20031027
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ES 2209639	A1	20040616	ES 2002-2502	20021031

ES 2209639	B1	20050801		
AU 2003272019	A1	20040525	AU 2003-272019	20031027
EP 1556361	A1	20050727	EP 2003-753860	20031027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006052625	A1	20060309	US 2005-532397	20050422
US 7179913	B2	20070220		
NO 2005002574	A	20050527	NO 2005-2574	20050527
PRIORITY APPLN. INFO.:			ES 2002-2502 A	20021031
			WO 2003-IB4763 W	20031027

OTHER SOURCE(S): CASREACT 140:391299
GI



I



II

AB A method for preparing the intermediate 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile (I; m.p. 180-183°) which comprises the condensation reaction of 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in a non-aqueous medium in the presence of methanesulfonic acid, which produces good I yields and short reaction times. I is cyclized into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (II; m.p. 217°) under reflux in an aliph alc. (e.g., ethanol) or alc.-water mixture

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:267313 HCAPLUS
DOCUMENT NUMBER: 140:303705
TITLE: Two-step process for the synthesis of high-purity 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine from 2,3-dichlorobenzoyl cyanide and aminoguanidine dimesylate

INVENTOR(S):	Neu, Jozsef; Gizur, Tibor; Toerley, Jozsef; Csabai, Janos; Vegh, Ferenc; Kalvin, Peter; Tarkanyi, Gabor	
PATENT ASSIGNEE(S):	Richter Gedeon Vegyeszeti Gyar Rt., Hung.	
SOURCE:	PCT Int. Appl., 12 pp. CODEN: PIXXD2	
DOCUMENT TYPE:	Patent	
LANGUAGE:	English	
FAMILY ACC. NUM. COUNT:	1	
PATENT INFORMATION:		

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026845	A1	20040401	WO 2003-HU72	20030918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
HU 200203114	A2	20040528	HU 2002-3114	20020920
CA 2498761	A1	20040401	CA 2003-2498761	20030918
AU 2003267676	A1	20040408	AU 2003-267676	20030918
EP 1539720	A1	20050615	EP 2003-748368	20030918
EP 1539720	B1	20061122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 346051	T	20061215	AT 2003-748368	20030918
IN 2005KN00267	A	20060714	IN 2005-KN267	20050224
US 2006178511	A1	20060810	US 2005-528379	20051129
PRIORITY APPLN. INFO.:			HU 2002-3114 A	20020920
			WO 2003-HU72 W	20030918

OTHER SOURCE(S): CASREACT 140:303705
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB High-purity 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (I; i.e., lamotrigine) is prepared by the condensation reaction of 2,3-dichlorobenzoyl cyanide (II) with 1-2 mol equivalent of an aminoguanidine salt (e.g., aminoguanidine dimesylate) in 3-6 mol equivalent of methanesulfonic acid, then the obtained adduct (III) is transformed without isolation into the desired product by contacting it with magnesium oxide, followed by crystallization of the product from an appropriate organic solvent (e.g., acetone).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:507707 HCAPLUS
DOCUMENT NUMBER: 139:69292
TITLE: Process for the preparation of lamotrigine and related 3,5-diamino-6-substituted-1,2,4-triazines via

cyclization of cyanoiminoguanidines.

INVENTOR(S):	Guntoori, Bhaskar Reddy; Che, Daqing; Murthy, K. S. Keshava
PATENT ASSIGNEE(S):	Brantford Chemicals Inc., Can.
SOURCE:	U.S., 11 pp. CODEN: USXXAM
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6586593	B1	20030701	US 2002-46383	20020116
CA 2366521	A1	20030624	CA 2001-2366521	20011224
CA 2366521	C	20070306		
WO 2003078407	A1	20030925	WO 2002-CA1926	20021218
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002367765	A1	20030929	AU 2002-367765	20021218
EP 1458692	A1	20040922	EP 2002-807048	20021218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
NZ 533734	A	20051223	NZ 2002-533734	20021218
PRIORITY APPLN. INFO.:			CA 2001-2366521 A	20011224
			WO 2002-CA1926 W	20021218

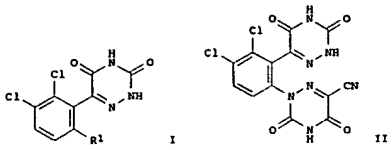
OTHER SOURCE(S): CASREACT 139:69292; MARPAT 139:69292
GI

I

AB Title compds. [I; R = (substituted) alkyl, aryl], were prepared by reaction of RCOCN with aminoguanidine in the presence of an organic sulfonic acid in an organic solvent under anhydrous conditions to give (HO)C(R)(CN)NHNC(NH2)2, dehydration of this to give NCC(R){:NN:C(NH2)2}, and cyclization of the latter. Thus, aminoguanidine hydrochloride in DMF was treated with MeSO3H and 2,3-dichlorobenzoyl chloride followed by stirring for 1 h, addition of SOCl2, and stirring for 1 h to give 39.2% iminoguanidine derivative The latter was refluxed with KOH in Me2CHOH to give 82% lamotrigine monohydrate.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:385795 HCAPLUS
DOCUMENT NUMBER: 140:199296
TITLE: Synthesis of oxo analogs of Lamotrigine and related compounds
AUTHOR(S): Hlavac, Jan; Buchtik, Roman; Slouka, Jan; Hradil, Pavel; Wiedermannova, Iveta
CORPORATE SOURCE: Department of Organic Chemistry, Palacky University, Olomouc, CZ-771 46, Czech Rep.
SOURCE: ARKIVOC (Gainesville, FL, United States) (2003), (1), 22-28
CODEN: AGFUAR
URL: http://www.arkat-usa.org/ark/journal/2003/General/2-556P/556P.pdf
PUBLISHER: Arkat USA Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:199296
GI



AB Lamotrigine oxo analogs I (R1 = H, Cl, Br, iodo, HO) were prepared from azauracil I (R1 = NH2) via the formation of the intermediate diazonium salt. Coupling of this diazonium salt with Et cyanoacetylcarbamate gave the corresponding carbamoyl hydrazone, which underwent intramol. cyclization upon reflux in pyridine to afford bis(triazinyl)benzene II containing two 6-azauracil rings.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:334829 HCAPLUS
DOCUMENT NUMBER: 138:343889
TITLE: Novel pharmaceutical compounds containing drugs bound to polypeptides
INVENTOR(S): Picariello, Thomas
PATENT ASSIGNEE(S): New River Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 4662 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 24
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003034980	A2	20030501	WO 2001-US43089	20011114
WO 2003034980	A3	20051103		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2428971	A1	20030501	CA 2001-2428971	20011114
EP 1401374	A1	20040331	EP 2001-274606	20011114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2006516948	T	20060713	JP 2003-537549	20011114
US 2004063628	A1	20040401	US 2002-156527	20020529
US 7060708	B2	20060613		
US 2007060500	A1	20070315	US 2006-392878	20060330
			US 2000-274622P	P 20001114
			US 1999-265415	B2 19990310
			US 1999-411238	B2 19991004
			WO 2000-US5693	A 20000306
			US 2000-642820	A2 20000822
			US 2000-247594P	P 20001114
			US 2000-247622P	P 20001114
			US 2000-247684P	P 20001114
			US 2000-248528P	P 20001116
			US 2000-248620P	P 20001116
			US 2000-248659P	P 20001116
			US 2000-248660P	P 20001116
			US 2000-248662P	P 20001116
			US 2000-248663P	P 20001116
			US 2000-248685P	P 20001116
			US 2000-248733P	P 20001116
			US 2000-248737P	P 20001116
			US 2000-248738P	P 20001116
			US 2000-248748P	P 20001116
			US 2000-248764P	P 20001116
			US 2000-248767P	P 20001116
			US 2000-248768P	P 20001116
			US 2000-248769P	P 20001116
			US 2000-248770P	P 20001116
			US 2000-248771P	P 20001116
			US 2000-248772P	P 20001116
			US 2000-248774P	P 20001116
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			US 2000-248778P	P 20001116
			US 2000-248779P	P 20001116
			US 2000-248782P	P 20001116
			US 2000-248787P	P 20001116
			US 2000-248794P	P 20001116
			US 2000-248795P	P 20001116
			US 2000-248796P	P 20001116
			US 2000-248797P	P 20001116
			US 2001-933708	A2 20010822

PRIORITY APPLN. INFO.:

			US 2001-986426	A2 20011108
			US 2001-987458	B2 20011114
			WO 2001-US43089	W 20011114
			US 2001-988034	B2 20011116
			US 2001-988071	B2 20011116
			WO 2001-US43115	B2 20011116
			WO 2001-US43117	B2 20011116
			US 2002-356381P	P 20020222
			US 2002-366258P	P 20020322
			US 2002-156527	A2 20020529
			US 2003-507012P	P 20030930
			US 2004-567800P	P 20040505
			US 2004-567802P	P 20040505
			US 2004-568011P	P 20040505
			US 2004-923088	A2 20040823
			WO 2004-US32131	A2 20040930

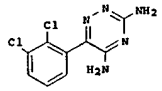
AB Compns. comprising polypeptides and drugs covalently attached to the polypeptide are disclosed. Also provided is a method for delivery of these drugs to a patient comprising administering to the patient a composition comprising a polypeptide and a drug covalently attached to the polypeptide. Also provided is a method for protecting drugs from degradation comprising covalently attaching them to a polypeptide. Also provided is a method for controlling release of drugs from a composition comprising covalently attaching them to the polypeptide.

L4 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:76761 HCAPLUS
DOCUMENT NUMBER: 138:137336
TITLE: Method for producing lamotrigine from alpha-oxo-2,3-dichlorophenylacetamidinoaminoguanidino hydrazone by ring closure reaction
INVENTOR(S): Schneider, Geza; Gegoe, Csaba Lehel; Ondi, Levente; Mate, Attila Gergely; Lukacs, Ferenc; Nyerges, Miklos; Garaczi, Sandor
PATENT ASSIGNEE(S): Helm AG, Germany; CP Pharma Gyogyszergyarto Kft.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

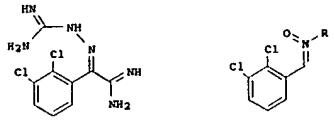
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008393	A1	20030130	WO 2002-EP7433	20020704
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10134980	A1	20030213	DE 2001-10134980	20010717
DE 10134980	C2	20030528		
EP 1311492	A1	20030521	EP 2002-758308	20020704
EP 1311492	B1	20040908		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, BG, CZ, EE				
CA 2417435	C	20040113	CA 2002-2417435	20020704
CA 2417435	A1	20030130		
ES 2224074	T3	20050301	ES 2002-2758308	20020704
US 2003191310	A1	20031009	US 2003-343225	20030515
US 6683182	B2	20040127		
			DE 2001-10134980	A 20010717
			WO 2002-EP7433	W 20020704

PRIORITY APPLN. INFO.:
OTHER SOURCE(S): CASREACT 138:137336; MARPAT 138:137336
GI



I

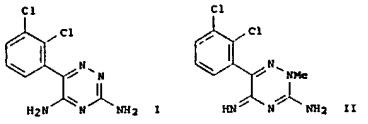


II III

AB The invention relates to a method for producing 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (lamotrigine (I)), or its pharmaceutically acceptable salts, by ring closure reaction from α-oxo-2,3-dichlorophenylacetamidinoaminoguanidino hydrazone (II) or its salts. The preparation of II from N-oxides, III (R = linear, branched or cyclic (un)substituted alkyl, aryl, aralkyl), or their salts, are also described. Thus, I was prepared from 2,3-Cl2C6H3CH:N(O)Ph, via cyanation with NaCN, amination to the acetamidine hydrochloride, reaction with aminoguanine bicarbonate to give II·HCl, treatment with aqueous NaOH to give the free base, which is cyclized to I; cyclization of II·HCl gives I·HCl.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:549382 HCAPLUS
DOCUMENT NUMBER: 138:24695
TITLE: Synthesis of stable isotopically labelled versions of Lamotrigine and its methylated metabolite
AUTHOR(S): Manning, Calvin O.; Wadsworth, Alan H.; Fellows, Ian

CORPORATE SOURCE: Chemical Development, GlaxoSmithKline Research and Development, Stevenage, SG1 2NY, UK
SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals (2002), 45(7), 611-618
CODEN: JLCRD4; ISSN: 0362-4803
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:24695
GI

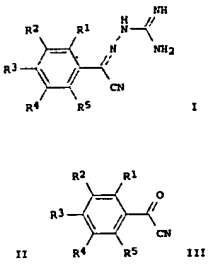


AB Lamotrigine (I) is a sodium channel antagonist used for the treatment of epilepsy. Stable isotopically labeled [M + 7] analogs of I and of its N-methylated metabolite II were prepared using [M + 5] labeled [13C, 15N4]-aminoguanidine, obtained from labeled thiourea. The overall yield for isotopically labeled II was 34% from [M + 3] labeled [13C, 15N2]-thiourea.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:631908 HCAPLUS
DOCUMENT NUMBER: 135:195578
TITLE: Process for preparing substituted benzoyl cyanide amidinohydrazones as intermediates for synthesis of 3,5-diamino-6-phenyl-1,2,4-triazines
INVENTOR(S): Nadaka, Vladimir; Lexner, Jael; Kaspi, Joseph
PATENT ASSIGNEE(S): Chemagis Ltd., Israel
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1127873	A2	20010829	EP 2001-103660	20010223
EP 1127873	A3	20030507		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
IL 134730	A	20031031	IL 2000-134730	20000225
CA 2337280	A1	20010825	CA 2001-2337280	20010215
HU 200100740	A2	20011128	HU 2001-740	20010215
US 2001025118	A1	20010927	US 2001-789634	20010222
US 6329521	B2	20011211		

PRIORITY APPLN. INFO.: IL 2000-134730 A 20000225
OTHER SOURCE(S): CASREACT 135:195578; MARPAT 135:195578
GI



AB The title compds. [I; R1-R5 = H, halo, alkyl, etc.], useful as intermediates for synthesis of 1,2,4-triazines II (active in the treatment of CNS disorders), were prepared by reacting the benzoyl cyanides III with aminoguanidine bicarbonate in a mixture of a water-soluble solvent and polyphosphoric acid. Thus, reacting 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in the presence of polyphosphoric acid in MeCN afforded 2,3-dichlorobenzoyl cyanide amidinohydrazone which was then heated under reflux in PrOH to give 2,3-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine.

L4 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:507682 HCAPLUS
DOCUMENT NUMBER: 135:108912
TITLE: Preparation of 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (lamotrigine)
INVENTOR(S): Radhakrishnan, Tarur Venkatasubramanian; Sasikumar, Thoovara Mohan; Srivastava, Anita Ranjan
PATENT ASSIGNEE(S): RPG Life Sciences Limited, India
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001049669	A1	20010712	WO 2000-IN1	20000103
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,				

SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

GB 2372988	A	20020911	GB 2002-14791	20000103
GB 2372988	B	20040407		
BR 2000016980	A	20021001	BR 2000-16980	20000103
DE 10085384	T0	20021212	DE 2000-10085384	20000103
DE 10085384	B4	20060614		
AU 763244	B2	20030717	AU 2000-44288	20000103
IN 2002MN00829	A	20040313	IN 2002-MN829	20020619
US 6639072	B1	20031028	US 2002-149429	20020624

PRIORITY APPLN. INFO.: WO 2000-IN1 A 20000103
AB The title compound was prepared by hydrogenation of 2,3-Cl2C6H3NO2 in MeOH at 80 psi H pressure using Raney Ni catalyst at 30° to give 2,3-Cl2C6H3NH2 which was diazotized and converted to nitrile with CuCN/NaCN at 65-70°. The resulting 2,3-Cl2C6H3CN was hydrolyzed to give 2,3-Cl2C6H3CO2 which was converted to acid chloride at 80° with SOCl2. The 2,3-Cl2C6H3COCl was cyano-dehalogenated with CuCN/KI by refluxing in PhCl under an inert atmospheric and the product 2,3-Cl2C6H3COCN was condensed with aminoguanidine bicarbonate in PhMe in the presence of H2SO4 and p-MeC6H4SO3H at 100-120°, followed by in-situ cyclization of the Schiff base by refluxing with MeONa in MeOH. Crude lamotrigine is purified by recrystn. from MeOH.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:369058 HCAPLUS
DOCUMENT NUMBER: 136:14957
TITLE: Isolation of lamotrigine 2-N-glucuronide from guinea pig urine
AUTHOR(S): Yeh, Shih-Woei; Yu, Hsiu-Ying
CORPORATE SOURCE: School of Pharmacy, National Taiwan University, Taipei, 100, Taiwan
SOURCE: Chinese Pharmaceutical Journal (Taipei, Taiwan) (2000), 52(5), 241-249
CODEN: CPHJEP; ISSN: 1016-1015
PUBLISHER: Pharmaceutical Society of Republic of China
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lamotrigine (LT) is a novel anticonvulsant. Its major metabolite in human is 2-N-glucuronide (LT-2NG). In order to investigate the metabolic characteristics of LT in our laboratory, a reference standard of LT-2NG was required.
The purpose of this experiment was to isolate pure LT-2NG from the urine of LT-treated guinea pigs. The pooled urine of guinea pigs fed with LT was eluted with methanol through XAD-2 column. LT-2NG in the eluent was purified by semi-preparative HPLC equipped with a C8 column and a UV detector set at 267 nm. The mobile phase for HPLC was 0.01M ammonium acetate (pH 6.6) containing 12% of methanol. The isolated LT-2NG was confirmed by mass, 1H NMR and 13C NMR spectroscopic anal. The mol. ion 432.1, a downfield anomeric proton at 5.39 ppm, and an upfield shift (-6.9 ppm) of the triazine ring C-3 indicate attachment of the glucuronide to the N-2 of LT. These spectra were identical with the reported spectra of LT-2NG isolated from human urine.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:421116 HCAPLUS
DOCUMENT NUMBER: 133:60362
TITLE: An improved process for preparation of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine
INVENTOR(S): Vyas, Sharad Kumar
PATENT ASSIGNEE(S): India
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035888	A1	20000622	WO 1999-IB1955	19991207
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IN 183150	A1	19990925	IN 1998-CA2171	19981214
CA 2334937	A1	20000622	CA 1999-2334937	19991207
CA 2334937	C	20040921		
AU 2000012924	A	20000703	AU 2000-12924	19991207
EP 1140872	A1	20011010	EP 1999-956293	19991207
EP 1140872	B1	20030917		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 250041	T	20031015	AT 1999-956293	19991207
RU 2231526	C2	20040627	RU 2001-115698	19991207

PRIORITY APPLN. INFO.: IN 1998-CA2171 A 19981214
WO 1999-IB1955 W 19991207
AB 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (lamotrigine) (I) useful as antiepileptic drug (no data) is prepared in a 3 step process. Thus, 2,3-dichlorobenzoylchloride was treated with cuprous cyanide in presence of acetonitrile and a solvent to produce 2,3-dichlorobenzoyl cyanide, further with aminoguanidine and cyclized to produce I.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:795469 HCAPLUS
DOCUMENT NUMBER: 132:26963
TITLE: Preparation of 1,2,4-triazine derivative, and its use as reference marker for testing purity and stability of lamotrigine
INVENTOR(S): Edmeades, Lorraine Mary; Griffith-Skinner, Nigel Arthur; Hill, Derek Anthony; Hill, Graham Thornton; Packham, Terrence William
PATENT ASSIGNEE(S): The Wellcome Foundation Limited, UK
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 963980	A2	19991215	EP 1999-200695	19990310
EP 963980	A3	20000531		
EP 963980	B1	20020605		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
SG 85628	A1	20020115	SG 1999-1252	19990325
MX 9902202	A	20000831	MX 1999-2202	19990305
KR 2000005611	A	20000125	KR 1999-7632	19990309
HR 990074	A1	20001031	HR 1999-74	19990309
ZA 9901951	A	19990816	ZA 1999-1951	19990310
JP 2989189	B2	19991213	JP 1999-63792	19990310
JP 2000009714	A	20000114		
NO 9901151	A	19991213	NO 1999-1151	19990310
CN 1238454	A	19991215	CN 1999-103445	19990310
AU 9920319	A	20000106	AU 1999-20319	19990310
TR 9900520	A2	20000121	TR 1999-520	19990310
HU 9900592	A2	20000428	HU 1999-592	19990310
BR 9900984	A	20000502	BR 1999-984	19990310
NZ 334590	A	20000728	NZ 1999-334590	19990310
CA 2265194	C	20001010	CA 1999-2265194	19990310
US 6333198	B1	20011225	US 1999-265670	19990310
EP 1170588	A1	20020109	EP 2001-203376	19990310
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 218552	T	20020615	AT 1999-200695	19990310
PT 963980	T	20021031	PT 1999-200695	19990310
ES 2178342	T3	20021216	ES 1999-200695	19990310
CN 1306210	A	20010801	CN 2000-122208	20000725
US 2002055177	A1	20020509	US 2001-940422	20010829
NO 2003002753	A	19991213	NO 2003-2753	20030617

PRIORITY APPLN. INFO.: GB 1998-12413 A 19980610; EP 1999-200695 A3 19990310; US 1999-265670 A3 19990310

AB A method of testing the purity or stability to degradation of a sample of lamotrigine or a pharmaceutical dosage form comprising lamotrigine consists of assaying the sample for the presence of a compound selected from 3-amino-6-(2,3-dichlorophenyl)-1,2,4-triazine-5-(4H)-one and N-[5-amino-6-(2,3-dichlorophenyl)-1,2,4-triazine-3-yl]-2,3-dichlorobenzamide (I). A process for producing compound I, is also disclosed. Lamotrigine was treated with 2,3-dichlorobenzoyl chloride to give I. TLC-densitometry was used to determine I in lamotrigine tablets.

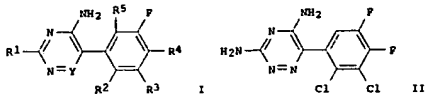
L4 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:473716 HCAPLUS
DOCUMENT NUMBER: 127:81468
TITLE: Fluorophenyl-triazine and pyrimidine derivatives as compounds acting on the central nervous system
INVENTOR(S): Torrens Jover, Antoni; Frigola Constansa, Jordi
PATENT ASSIGNEE(S): Laboratorios Del Dr. Esteve, S.A., Spain; Torrens Jover, Antoni; Frigola Constansa, Jordi
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9720827	A1	19970612	WO 1996-EP5593	19961204
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2741879	A1	19970606	FR 1995-14354	19951205
AU 9711943	A	19970627	AU 1997-11943	19961204
ES 2128960	A1	19990516	ES 1996-2667	19961205
ES 2128960	B1	20000116		

PRIORITY APPLN. INFO.: FR 1995-14354 A 19951205; WO 1996-EP5593 W 19961204

OTHER SOURCE(S): CASREACT 127:81468; MARPAT 127:81468
GI



AB Novel fluorophenyl-triazine and pyrimidine derivs. I and their physiol. acceptable salts are disclosed [wherein R1 = amino, 1-piperazinyl or 4-alkylpiperazin-1-yl, where alkyl = C1-4 chain, preferably Me; R2, R3, R4 = halo, preferably F or Cl; R5 = H or halo, preferably F or Cl; Y = N, CH]. A method for preparing the compds. is also disclosed, as are pharmaceutical compns. containing a pharmaceutically acceptable carrier and at least one such compound The compds. are CNS agents which act by inhibiting the release of glutamate. Examples include 13 syntheses, 1 standard formulation, and biol. data for 5 compds. For instance, 2,3-dichloro-4,5-difluorobenzoic acid (prepared in 3 steps) was converted to the acid chloride (99%) and then to the acyl cyanide (98%), and the latter was condensed with aminoguanidine bicarbonate and cyclized (31%) to give title compound II. In a test for prevention of hypoxic death in mice, II had an ED50 of 0.6 mg/kg i.p., vs. 1.2 mg/kg for lamotrigine.

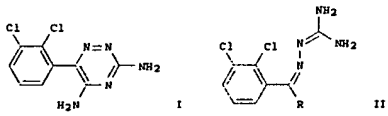
L4 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:548552 HCAPLUS
DOCUMENT NUMBER: 125:195694
TITLE: Preparation of lamotrigine.
INVENTOR(S): Winter, Raymond Geoffrey; Sawyer, David Alan; Germain, Andrew
PATENT ASSIGNEE(S): Wellcome Foundation Limited, UK
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9620934	A1	19960711	WO 1995-GB3048	19951229
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9643115	A	19960724	AU 1996-43115	19951229
EP 800520	A1	19971015	EP 1995-941817	19951229
EP 800520	B1	20020619		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
HU 77346	A2	19980330	HU 1997-1867	19951229
HU 224688	B1	20051228		
JP 11501007	T	19990126	JP 1995-520803	19951229
RU 2145602	C1	20000220	RU 1997-112881	19951229
AT 219487	T	20020715	AT 1995-941817	19951229
PT 800520	T	20021129	PT 1995-941817	19951229
ES 2177672	T3	20021216	ES 1995-941817	19951229
FI 9702719	A	19970827	FI 1997-2719	19970624
US 5912345	A	19990615	US 1997-836153	19970625

PRIORITY APPLN. INFO.: GB 1994-26439 A 19941230; GB 1994-26447 A 19941230; WO 1995-GB3048 W 19951229

OTHER SOURCE(S): CASREACT 125:195694; MARPAT 125:195694
GI



AB Lamotrigine (I) was prepared by irradiation of (II; R = CN, CONH2) with UV or visible radiation in an organic solvent, or, when R = CN, by heating. Thus, II (R = CN) was refluxed in 1-propanol under irradiation from a medium pressure Hg lamp for 8 h to give 73% lamotrigine.

L4 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:546365 HCAPLUS
DOCUMENT NUMBER: 125:195693
TITLE: Preparation of lamotrigine.
INVENTOR(S): Lee, Grahame Roy
PATENT ASSIGNEE(S): Wellcome Foundation Limited, UK
SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9620935	A1	19960711	WO 1995-GB3049	19951229
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9643116	A	19960724	AU 1996-43116	19951229
EP 800521	A1	19971015	EP 1995-941818	19951229
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
HU 77347	A2	19980330	HU 1997-1875	19951229
JP 11507011	T	19990622	JP 1995-520618	19951229
RU 2162081	C2	20010120	RU 1997-112921	19951229
FI 9702720	A	19970827	FI 1997-2720	19970624
US 5925755	A	19990720	US 1997-836152	19970625

PRIORITY APPLN. INFO.: GB 1994-26448 A 19941230; WO 1995-GB3049 W 19951229

AB Lamotrigine, 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (I), is prepared by treating 6-(2,3-dichlorophenyl)-5-chloro-3-thiomethyl-1,2,4-triazine (II) with NH3. Thus, II (preparation given) was heated with ethanolic NH3 in a sealed tube at 180° and 280 psi for 72 h to give I.

L4 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:128970 HCAPLUS
DOCUMENT NUMBER: 116:128970
TITLE: Preparation of 6-aminophenyl-3,5-diamino-1,2,4-triazines as neuroprotective agents
INVENTOR(S): Leach, Michael John; Nobbs, Malcolm Stuart
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 459829	A1	19911204	EP 1991-304962	19910531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 9104158	A	19930301	ZA 1991-4158	19910530
CA 2043642	A1	19911202	CA 1991-2043642	19910531
FI 9102622	A	19911202	FI 1991-2622	19910531
AU 9178099	A	19911205	AU 1991-78099	19910531
AU 630811	B2	19921105		
HU 60726	A2	19921028	HU 1991-1827	19910531
JP 06025193	A	19940201	JP 1991-235335	19910531

PRIORITY APPLN. INFO.: GB 1990-12312 A 19900601
OTHER SOURCE(S): MARPAT 116:128970

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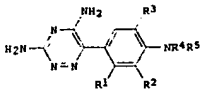

I

AB Title compds. (I; 1 of R1-R3 = Cl and the others = H or Cl; R4, R5 = H, alkyl) were prepared Thus, 2,5,3-Cl2(H2N)C6H2CO2H was converted in 3 steps to 2,3,5-Cl3C6H2COCN which was cyclocondensed with H2NC(:NH)NHNH2 and the product nitrated to give, after reduction, I (R1-R3 = Cl, R4 = R5 = H). The latter had IC50 of <10 μM against glutamate release from rat brain slices.

L4 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:112505 HCAPLUS
DOCUMENT NUMBER: 108:112505
TITLE: Preparation of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine isethionate as an antiepileptic
INVENTOR(S): Sawyer, David Alan; Copp, Frederick Charles
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 5 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 247892	A1	19871202	EP 1987-304776	19870529
EP 247892	B1	19910424		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DK 8702759	A	19871201	DK 1987-2759	19870529
DK 166278	B	19930329		
DK 166278	C	19930823		
FI 8702406	A	19871201	FI 1987-2406	19870529
FI 90770	B	19931215		
FI 90770	C	19940325		
AU 8773684	A	19871203	AU 1987-73684	19870529
AU 597982	B2	19900614		
JP 62289570	A	19871216	JP 1987-134772	19870529
JP 07051571	B	19950605		
HU 45978	A2	19880928	HU 1987-2487	19870529
HU 196769	B	19890130		
ZA 8703896	A	19890125	ZA 1987-3896	19870529
US 4847249	A	19890711	US 1987-56136	19870529
AT 62902	T	19910515	AT 1987-304776	19870529
CA 1286670	C	19910723	CA 1987-538395	19870529
IL 82710	A	19920115	IL 1987-82710	19870529
PRIORITY APPLN. INFO.:			GB 1986-13183 A	19860530
			EP 1987-304776 A	19870529

AB The title compound (I.isethionate), useful as an anticonvulsant (no data),

was prepared by reaction of I with 2-hydroxyethanesulfonic acid (II) or by reaction of I salts with the anion of II. A 1.0 M solution of Na isethionate in H2O was passed through a column of IR 120 (H) ion exchange resin. I (preparation given) was added to the resulting II and the solution was filtered and evaporated Recrystn. from industrial methylated spirit gave 72% I.isethionate.

L4 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:542021 HCAPLUS
DOCUMENT NUMBER: 103:142021
TITLE: Triazine compounds having cardiovascular activity
INVENTOR(S): Allan, Geoffrey; Miller, Alastair Ainslie; Sawyer, David Alan
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 142306	A2	19850522	EP 1984-307374	19841026
EP 142306	A3	19861120		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4649139	A	19870310	US 1984-663682	19841022
DK 8405121	A	19850428	DK 1984-5121	19841026
FI 8404212	A	19850428	FI 1984-4212	19841026
AU 8434758	A	19850509	AU 1984-34758	19841026
AU 564667	B2	19870820		
JP 60109577	A	19850615	JP 1984-225636	19841026
DD 224033	A5	19850626	DD 1984-268757	19841026
HU 36102	A2	19850828	HU 1984-4003	19841026
HU 191566	B	19870330		
ES 537104	A1	19860416	ES 1984-537104	19841026
ZA 8408388	A	19860625	ZA 1984-8388	19841026
SU 1371500	A3	19880130	SU 1984-3805251	19841026
IL 73332	A	19880630	IL 1984-73332	19841026
PL 144899	B1	19880730	PL 1984-250213	19841026
CA 1261328	A1	19890926	CA 1984-466473	19841026
PRIORITY APPLN. INFO.:			GB 1983-28757 A	19831027
OTHER SOURCE(S):	MARPAT 103:142021			

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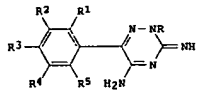

I

AB Tautomeric iminotriazinamines I [R = (un)substituted C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, C3-10 cycloalkyl; R1-R5 = H, halogen, alkenyloxy, acyl, acyloxy, cyano, NO2, aryl, alkylthio, (un)substituted alkyl,

alkenyl, alkynyl, alkoxy, amino; R1R2, R2R3, R3R4, R4R5 = CH:CHCH:CH] were prepared Thus, 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine was alkylated with Me2CHI to give I-HI (R = Me2CH, R1 = R2 = Cl; R3-R5 = H) which was converted to the mesylate salt (II) (12% overall yield). II at 1 mg/kg i.v. to rats increased the amount of aconitine required to elicit ventricular arrhythmias by 490% compared with 84% for 1 mg/kg verapamil.

L4 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:89397 HCAPLUS
DOCUMENT NUMBER: 98:89397
TITLE: Substituted aromatic compounds
INVENTOR(S): Baxter, Martin G.; Elphick, Albert R.; Miller, Alistair A.; Sawyer, David A.
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Can., 26 pp. Division of Can. Appl. No. 353,081.
CODEN: CAXXA4
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 1133938	A2	19821019	CA 1981-373126	19810316
CA 1112643	A1	19811117	CA 1980-353081	19800530
US 4486354	A	19841204	US 1981-308805	19811005
AU 566870	B2	19871105	AU 1983-14051	19830428
US 4602017	A	19860722	US 1984-583286	19840227
FI 8400888	A	19840306	FI 1984-888	19840306
FI 73203	B	19870529		
FI 73203	C	19870910		
PRIORITY APPLN. INFO.:			GB 1979-19257 A	19790601
			CA 1980-353081 A3	19800530
			US 1980-154198 A1	19800529
			FI 1980-1758 A	19800530
			CA 1981-373126	19810316
			US 1981-302365 A1	19810915

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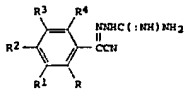

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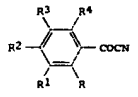
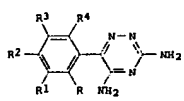


II



III

AB [(Cyanobenzylidene)amino]guanidines I (R-R4 = H, halo, alkyl, F3C; RR1 = HC:CHCH:CH, halobenzo, trifluoromethylbenzo, alkylbenzo) were prepared from the benzoyl cyanides II and H2NNHC(:NH)NH2 and were useful as intermediates in the preparation of anticonvulsant triazines III. Thus, 2,3-Cl2C6H3COCl was treated with CuCN to give 2,3-Cl2C6H3COCN which was treated with H2NNHC(:NH)NH2 to give I (R = R1 = Cl, R2 = R3 = R4 = H), which was cyclized by KOH to give III (R = R2 = Cl, R2 = R3 = R4 = H) (IV). The anticonvulsant ED50 of IV was 2.4 mg/kg in the maximal electroshock test.

L4 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:208914 HCAPLUS
DOCUMENT NUMBER: 94:208914
TITLE: 1,2,4-Triazine derivatives, pharmaceutical compositions and intermediates utilized for their preparation
INVENTOR(S): Baxter, Martin George; Elphick, Albert Reginald; Miller, Alistair Ainslie; Sawyer, David Alan
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 21121	A1	19810107	EP 1980-103032	19800530
EP 21121	B1	19830511		
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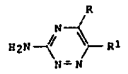
DK 8002338	A	19801202	DK 1980-2338	19800530
DK 153787	B	19880905		
DK 153787	C	19890116		
FI 8001758	A	19801202	FI 1980-1758	19800530
FI 67844	B	19850228		
FI 67844	C	19850610		
AU 8058906	A	19801204	AU 1980-58906	19800530
AU 530999	B2	19830804		
JP 56025169	A	19810310	JP 1980-71580	19800530
JP 01044706	B	19890929		
ES 491998	A1	19810516	ES 1980-491998	19800530
DD 151309	A5	19811014	DD 1980-221474	19800530
ZA 8003250	A	19820127	ZA 1980-3250	19800530
AT 8002896	A	19820715	AT 1980-2896	19800530
AT 370097	B	19830225		
EP 59987	A1	19820915	EP 1982-102293	19800530
EP 59987	B1	19850814		
R: BE, CH, DE, FR, GB, LU, NL, SE				
PL 124029	B1	19821231	PL 1980-224633	19800530
HU 24621	A2	19830328	HU 1980-1364	19800530
HU 182086	B	19831228		
IL 60201	A	19840531	IL 1980-60201	19800530
CS 234018	B2	19850314	CS 1980-3829	19800530
SU 1055331	A3	19831115	SU 1980-2932704	19800602
US 4486354	A	19841204	US 1981-308805	19811005
US 4602017	A	19860722	US 1984-583286	19840227
FI 8400888	A	19840306	FI 1984-888	19840306

	FI 73203	B	19870529		
	FI 73203	C	19870910		
	JP 61033163	A	19860217	JP 1985-121370	19850604
	JP 01044179	B	19890926		
PRIORITY APPLN. INFO.:				GB 1979-19257 A	19790601
				US 1980-154198 A1	19800529
				EP 1980-103032 A	19800530
				FI 1980-1758 A	19800530
				US 1981-302365 A1	19810915

OTHER SOURCE(S): MARPAT 94:208914
G1



I

AB Triazines I (R = NH2, acylamino, aminomethyleneamino; R1 = substituted Ph) were prepared Thus, 2,3-Cl2C6H3I was Grignard carboxlated and the 2,3-Cl2C6H3CO2H converted to the chloride and treated with CuCN to give 2,3-Cl2C6H3COCN which was cyclized with aminoguanidine bicarbonate to I (R = NH2, R1 = 2,3-Cl2C6H3). The latter compound had an anticonvulsant ED50 of 2.4 mg/kg orally in mice.

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L6    1 ANSWERS   HCAPLUS  COPYRIGHT 2007 ACS on STN
IC    ICM  A61K
CC    63-6 (Pharmaceuticals)
TI    Pharmaceutical composition containing lamotrigine particles of defined
      morphology
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ST    lamotrigine particle morphol seizure treatment
IT    Phenols, biological studies
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (1,6-dialkyl; pharmaceutical composition containing lamotrigine particles of
         defined morphol. and excipients)
IT    Alcohols, biological studies
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (C16-18; pharmaceutical composition containing lamotrigine particles of
defined
         morphol. and excipients)
IT    Quaternary ammonium compounds, biological studies
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (alkylbenzyldimethyl, chlorides; pharmaceutical composition containing
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IT    Drug delivery systems
         (liqs., oral; pharmaceutical composition containing lamotrigine particles of
         defined morphol. and excipients)
IT    Drug delivery systems
         (particles; pharmaceutical composition containing lamotrigine particles of
         defined morphol. and excipients)
IT    Acacia
      Anticonvulsants
      Chondrules
      Egg yolk
      Human
      Seizures
         (pharmaceutical composition containing lamotrigine particles of defined
morphol.
         and excipients)
IT    Alcohols, biological studies
      Bentonite, biological studies
      Carbohydrates, biological studies
      Caseins, biological studies
      Gelatins, biological studies
      Kaolin, biological studies
      Polyoxyalkylenes, biological studies
      Tocopherols
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (pharmaceutical composition containing lamotrigine particles of defined
morphol.
         and excipients)
IT    Drug delivery systems
         (solids, oral; pharmaceutical composition containing lamotrigine particles
of
         defined morphol. and excipients)
IT    Fats and Glyceridic oils, biological studies
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (vegetable, hydrogenated; pharmaceutical composition containing lamotrigine
         particles of defined morphol. and excipients)
IT    Fats and Glyceridic oils, biological studies
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (vegetable; pharmaceutical composition containing lamotrigine particles of
         defined morphol. and excipients)
IT    9003-01-4D, crosslinked
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         (Carbomer; pharmaceutical composition containing lamotrigine particles of
         defined morphol. and excipients)
IT    9003-39-8D, crosslinked
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
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         (Crospovidone; pharmaceutical composition containing lamotrigine particles
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         defined morphol. and excipients)
IT    99-96-7D, alkyl esters
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (Parabens; pharmaceutical composition containing lamotrigine particles of
         defined morphol. and excipients)
IT    7631-86-9, Colloidal silicon dioxide, biological studies
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (colloidal; pharmaceutical composition containing lamotrigine particles of
         defined morphol. and excipients)
IT    9004-34-6, Cellulose, biological studies
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (microcryst.; pharmaceutical composition containing lamotrigine particles of
         defined morphol. and excipients)
IT    50-21-5, Lactic acid, biological studies  50-70-4, Sorbitol, biological
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      biological studies  57-15-8, Chlorobutanol  57-48-7, Fructose,
      biological studies  57-50-1, Sucrose, biological studies  57-55-6,
      Propylene glycol, biological studies  57-88-5, Cholesterol, biological
      studies  60-00-4, Ethylenediamine tetraacetic acid, biological studies
      60-12-8, Phenethyl alcohol  63-42-3, Lactose  64-17-5, Ethyl alcohol,
      biological studies  64-19-7, Acetic acid, biological studies  69-65-8,
      Mannitol  72-17-3, Sodium lactate  77-92-9, Citric acid, biological
      studies  79-41-4D, Methacrylic acid, polymers  81-07-2, Saccharin
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      108-32-7, Propylene carbonate  121-54-0, Benzethonium chloride
      127-09-3, Sodium acetate  128-37-0, Butylated hydroxy toluene, biological
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      1327-43-1, Magnesium aluminum silicate  7447-40-7, Potassium chloride,
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      chloride, biological studies  7681-57-4, Sodium metabisulfite
      7758-87-4, Tribasic calcium phosphate  7778-18-9, Calcium sulfate
      7789-77-7, Dibasic calcium phosphate dihydrate  8013-17-0, Invert sugar
      8027-56-3, Liquid glucose  9000-30-0, Guar gum  9000-65-1, Tragacanth
      9000-69-5, Pectin  9002-89-5, Polyvinyl alcohol  9003-39-8, Povidone
      9004-32-4, Carboxymethylcellulose sodium  9004-53-9, Dextrin  9004-57-3,
      Ethyl cellulose  9004-62-0, Hydroxyethyl cellulose  9004-64-2,
      Hydroxypropyl cellulose  9004-65-3, Hydroxypropyl methylcellulose
      9004-67-5, Methylcellulose  9005-25-8, Starch, biological studies
      9005-32-7, Alginic acid  9005-37-2, Propylene glycol alginate
      9005-38-3, Sodium alginate  9050-04-8  9050-36-6, Maltodextrin
      9063-38-1, Sodium starch glycolate  11138-66-2, Xanthan gum  14807-96-6,
      Talc, biological studies  22839-47-0, Aspartame  25013-16-5, Butylated
      hydroxyanisole  25322-68-3, Polyethylene glycol  36653-82-4, Cetyl
      alcohol  39404-33-6, Dextrates  54182-62-6D, Polacrilin, potassium form
      74811-65-7, Croscarmellose sodium  84057-84-1, Lamotrigine
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (pharmaceutical composition containing lamotrigine particles of defined
morphol.
         and excipients)

ALL ANSWERS HAVE BEEN SCANNED

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L5             0 S E3/RN
L6             1 S E3

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CA SUBSCRIBER PRICE                                   -19.50      -19.50

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DICTIONARY FILE UPDATES:   3 APR 2007  HIGHEST RN 929074-02-2

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L6              1 S E3

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
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FILE LAST UPDATED: 3 Apr 2007  (20070403/ED)

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 substance identification.

=> s lamotrigine/cn
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Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.




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         35536 "DIAMINO"
             3 "DIAMINOS"
         35536 "DIAMINO"
                 ("DIAMINO" OR "DIAMINOS")
       3871969 "6"
       9105408 "2"
       6859857 "3"
         15829 "DICHLOROPHENYL"
       9078625 "1"
       9105408 "2"
       5555409 "4"
         41884 "TRIAZINE"
         10234 "TRIAZINES"
         44464 "TRIAZINE"
                 ("TRIAZINE" OR "TRIAZINES")
L10         27 "3,5-DIAMINO-6-(2,3-DICHLOROPHENYL)-1,2,4-TRIAZINE"
                 ("3"(W)"5"(W)"DIAMINO"(W)"6"(W)"2"(W)"3"(W)"DICHLOROPHENYL"(W)
                 "1"(W)"2"(W)"4"(W)"TRIAZINE")


=> d scan l10 1-5
'1-5' IS NOT A VALID FORMAT FOR FILE 'HCAPLUS'

L10   27 ANSWERS   HCAPLUS  COPYRIGHT 2007 ACS on STN
IC    ICM  C07D253-06
      ICS  A61K031-53
CC    28-19 (Heterocyclic Compounds (More Than One Hetero Atom))
      Section cross-reference(s): 1, 63
TI    Preparation of 3,5-diamino-6-(
      2,3-dichlorophenyl)-1,2,
      4-triazine isethionate as an antiepileptic
ST    aminodichlorophenyltriazine isethionate prepn anticonvulsant; triazine
      diaminodichlorophenyl isethionate prepn anticonvulsant
IT    Anticonvulsants and Antiepileptics
         (diamino(dichlorophenyl)triazine.isethionate)
IT    6574-97-6, 2,3-Dichlorophenyl cyanide
      RL: RCT (Reactant); RACT (Reactant or reagent)
         (cyclocondensation of, with aminoguanidine)
IT    2582-30-1, Aminoguanidine bicarbonate
      RL: RCT (Reactant); RACT (Reactant or reagent)
         (cyclocondensation of, with dichlorophenyl cyanide)
IT    84057-84-1P
      RL: SPN (Synthetic preparation); PREP (Preparation)
         (preparation and conversion of, into isethionate salt)
IT    113170-86-8P
      RL: BAC (Biological activity or effector, except adverse); BSU (Biological
      study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
      BIOL (Biological study); PREP (Preparation); USES (Uses)
         (preparation of, as anticonvulsant)
IT    107-36-8, Isethionic acid
      RL: PROC (Process)
         (salt formation of, with diaminotriazine derivative)


The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
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CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
CLASS ------- IPC, NCL, ECLA, FTERM
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers;
              SCAN must be entered on the same line as the DISPLAY,
              e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, CLASS

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT)
              containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and
              its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and
              its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

To display a particular field or fields, enter the display field
codes.  For a list of the display field codes, enter HELP DFIELDS at
an arrow prompt (=>).  Examples of formats include: TI; TI,AU; BIB,ST;
TI,IND; TI,SO.  You may specify the format fields in any order and the
information will be displayed in the same order as the format
specification.

All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR,
FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC
to view a specified Accession Number.
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):ide
'IDE' IS NOT VALID HERE

To display more answers, enter the number of answers you would like to
see.  To end the display, enter "NONE", "N", "0", or "END".
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HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):5

L10   27 ANSWERS   HCAPLUS  COPYRIGHT 2007 ACS on STN
IC    ICM  A61K031-00
      ICS  C07D263-32
TI    Process for the preparation of 3,5-diamino-
      6-(2,3- dichlorophenyl)-1,
      2,4-triazine

L10   27 ANSWERS   HCAPLUS  COPYRIGHT 2007 ACS on STN
CC    75 (Crystallography and Liquid Crystals)
TI    Lamotrigine dimethylformamide sesquisolvate

L10   27 ANSWERS   HCAPLUS  COPYRIGHT 2007 ACS on STN
CC    25-20 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
TI    Synthesis of 2,3-Dichlorobenzonitrile
ST    dichloroaniline diazotization; dichlorophenyldiazinium prepn Sandmeyer
      reaction; dichlorobenzonitrile prepn
IT    Substitution reaction
         (Sandmeyer; preparation of dichlorobenzonitrile via diazotization of
         dichloroaniline followed by Sandmeyer reaction)
IT    608-27-5, 2,3-Dichloroaniline
      RL: RCT (Reactant); RACT (Reactant or reagent)
         (preparation of dichlorobenzonitrile via diazotization of dichloroaniline
         followed by Sandmeyer reaction)
IT    73260-77-2P
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
         (preparation of dichlorobenzonitrile via diazotization of dichloroaniline
         followed by Sandmeyer reaction)
IT    6574-97-6P, 2,3-Dichlorobenzonitrile
      RL: SPN (Synthetic preparation); PREP (Preparation)
         (preparation of dichlorobenzonitrile via diazotization of dichloroaniline
         followed by Sandmeyer reaction)

L10   27 ANSWERS   HCAPLUS  COPYRIGHT 2007 ACS on STN
IC    ICM  C07C281-18
CC    28-19 (Heterocyclic Compounds (More Than One Hetero Atom))
      Section cross-reference(s): 45
TI    Process for preparing 2-(2,3-dichlorophenyl)-2-
      (aminoguanidine)acetonitrile and a process for its cyclization into
      3,5-diamino-6-(2,3
      -dichlorophenyl)-1,2,4-
      triazine
ST    diaminodichlorophenyltriazine prepn cyclization
      dichlorophenylaminoguanidineacetonitrile
IT    Alcohols, uses
      RL: NUU (Other use, unclassified); USES (Uses)
         (aliphatic, solvents; in the cyclization of 2-(2,3-dichlorophenyl)-2-
         (aminoguanidine)acetonitrile into 3,5-
         diamino-6-(2,3-
         dichlorophenyl)-1,2,4-
         triazine)
IT    Condensation reaction catalysts
         (methanesulfonic acid; for the conversion of 2,3-dichlorobenzoyl
         cyanide with aminoguanidine bicarbonate in a non-aqueous medium to give
         2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile)
IT    Condensation reaction
         (of 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in a
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non-aqueous medium in the presence of methanesulfonic acid to give 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile)
IT Cyclization
(of 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine)
IT 75-75-2, Methanesulfonic acid
RL: CAT (Catalyst use); USES (Uses)
(condensation catalyst; in a process for preparing 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile from 2,3-dichlorobenzoyl cyanide and aminoguanidine bicarbonate)
IT 2582-30-1, Aminoguanidine bicarbonate 77668-42-9, 2,3-Dichlorobenzoyl cyanide
RL: RCT (Reactant); RACT (Reactant or reagent)
(in a process for preparing 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile)
IT 1310-73-2, Sodium hydroxide, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(in the condensation of 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in a non-aqueous medium in the presence of methanesulfonic acid to give 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile)
IT 84689-20-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparing 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile and a process for its cyclization into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine)
IT 84057-84-1P, 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for preparing 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile and a process for its cyclization into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine)
IT 64-17-5, Ethanol, uses 67-63-0, Isopropanol, uses 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; in the cyclization of 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine)

L10 27 ANSWERS HCAPLUS COPYRIGHT 2007 ACS on STN
CC 1-2 (Pharmacology)
TI Transplacental passage of lamotrigine in a human placental perfusion system in vitro and in maternal and cord blood in vivo
ST lamotrigine anticonvulsant bioavailability placenta perfusion pregnancy fetus epilepsy
IT Embryo, animal
(fetus; lamotrigine transplacental passage in human placental perfusion system in vitro and in maternal and cord blood in vivo)
IT Anticonvulsants
Drug bioavailability

Epilepsy
Human
Perfusion
Placenta
Pregnancy
(lamotrigine transplacental passage in human placental perfusion system in vitro and in maternal and cord blood in vivo)
IT Biological transport
(uptake; lamotrigine transplacental passage in human placental perfusion system in vitro and in maternal and cord blood in vivo)
IT 84057-84-1, Lamotrigine
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lamotrigine transplacental passage in human placental perfusion system in vitro and in maternal and cord blood in vivo)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> d his

(FILE 'HOME' ENTERED AT 16:55:13 ON 04 APR 2007)

FILE 'REGISTRY' ENTERED AT 16:55:37 ON 04 APR 2007
L1 STRUCTURE UPLOADED
L2 3 S L1 SSS SAM
L3 128 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 16:56:47 ON 04 APR 2007
L4 25 S L3/P
E US20050238724/PN,PRN,AN
L5 0 S E3/RN
L6 1 S E3

FILE 'REGISTRY' ENTERED AT 16:58:38 ON 04 APR 2007
L7 0 S L6

FILE 'HCAPLUS' ENTERED AT 17:00:04 ON 04 APR 2007
E LAMOTRIGINE+ALL/CT
S LAMOTRIGINE/CN

FILE 'REGISTRY' ENTERED AT 17:00:26 ON 04 APR 2007
L8 1 S LAMOTRIGINE/CN

FILE 'HCAPLUS' ENTERED AT 17:00:27 ON 04 APR 2007
L9 1265 S L8
L10 27 S 3,5-DIAMINO-6-(2,3-DICHLOROPHENYL)-1,2,4-TRIAZINE"

=> d l10 1-27 ibib abs

L10 ANSWER 1 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:365185 HCAPLUS
TITLE: Process for the preparation of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine
INVENTOR(S): Rawalnath, Sakhardande Rajiv; Kanji, Khatri Navin; Nilkanth, Firake Pandharinath; Vasant, Panchal Rajesh; Nagesh, Barekar Chandan; Madhukar, Mohite Dhanaji
PATENT ASSIGNEE(S): Saxena, Alok, India

SOURCE: Indian Pat. Appl.
CODEN: INXXBQ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 2006MU00071	A	20060421	IN 2006-MU71	20060117
PRIORITY APPLN. INFO.:			IN 2006-MU71	20060117

AB There is disclosed an improved process for the preparation of 3,5- diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine which process comprises the step of reacting 2,3-dichlorobenzoylchloride with cuprous cyanide in presence of acetonitrile without the need of a co solvent to obtain dichlorbenzoyl cyanide, said dichlorobenzoyl cyanide is reacted with amino guanidine bicarbonate to produce a schiff;s base, which is cyclized in presence of aqueous potassium hydroxide to produce 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine.

L10 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:40805 HCAPLUS
TITLE: Crystal structure of lamotriginium hydrogen phthalate dimethylformamide solvate (1:1:1)
AUTHOR(S): Sridhar, Balasubramanian; Ravikumar, Krishnan
CORPORATE SOURCE: Lab. X-ray Crystallography, Indian Inst. Chemical Technology, Hyderabad, India
SOURCE: Molecular Crystals and Liquid Crystals (2006), 461, 131-141
CODEN: MCLCD8; ISSN: 1542-1406
PUBLISHER: Taylor & Francis, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The title compound, 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine-hydrogen phthalate-dimethylformamide, $C_9H_8N_5Cl_2 \cdot C_8H_5O_4 \cdot C_3H_7NO$ (lamaphthalate), crystallizes in the triclinic space group P1 with unit cell parameters a = 10.1587(6) Å, b = 11.3704(7) Å, c = 12.1976(7) Å, α = 110.797(1)°, β = 111.61(1)°, γ = 99.53(1)°, V = 1151.16(12) Å3, and Z = 2. The asym. unit comprises one lamotriginium cation, one hydrogen phthalate anion, and one DMF solvate. The dihedral angle between the two planar rings is 65.3(1)°. The expected proton transfer occurs at N2 of the triazine ring. Both O-H...O and N-H...O hydrogen bonding stabilizes the crystal structure.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1032885 HCAPLUS
TITLE: Lamotrigine dimethylformamide sesquisolvate
AUTHOR(S): Sridhar, Balasubramanian; Ravikumar, Krishnan
CORPORATE SOURCE: Laboratory of X-ray Crystallography, Indian Institute of Chemical Technology, Hyderabad, 500 007, India

SOURCE: Acta Crystallographica, Section E: Structure Reports Online (2006), E62(10), o4752-o4754
CODEN: ACSEBH; ISSN: 1600-5368
URL: http://journals.iucr.org/e/issues/2006/10/00/is2071/index.html
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB In the title compound, $C_9H_7N_5Cl_2 \cdot 1.5C_3H_7NO$, the asym. unit consists of two crystallog. independent lamotrigine (systematic name: 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine) and three DMF mols. In the crystal structure, N-H···N and N-H···O hydrogen bonds lead to the formation of R22(8) and R23(8) motifs.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:421792 HCAPLUS
DOCUMENT NUMBER: 142:430313
TITLE: Process for preparation of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (Lamotrigine) via reaction of 2,3-dichlorobenzoyl chloride with cuprous cyanide and then with aminoguanidine bicarbonate followed by cyclization.
INVENTOR(S): Vyas, Sharad Kumar
PATENT ASSIGNEE(S): Torrent Pharmaceuticals Ltd., India
SOURCE: Indian, 12 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 183150	A1	19990925	IN 1998-CA2171	19981214
CA 2334937	A1	20000622	CA 1999-2334937	19991207
CA 2334937	C	20040921		
WO 2000035888	A1	20000622	WO 1999-IB1955	19991207
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000012924	A	20000703	AU 2000-12924	19991207
EP 1140872	A1	20011010	EP 1999-956293	19991207
EP 1140872	B1	20030917		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 250041	T	20031015	AT 1999-956293	19991207
RU 2231526	C2	20040627	RU 2001-115698	19991207
US 6111101	A	20000829	US 1999-456501	19991208

PRIORITY APPLN. INFO.: IN 1998-CA2171 A 19981214
WO 1999-IB1955 W 19991207

OTHER SOURCE(S): CASREACT 142:430313

AB Lamotrigine was prepared by reaction of 2,3-dichlorobenzoyl chloride with CuCN (1:1-2 molar ratio) in MeCN and a cosolvent to produce dichlorobenzoyl cyanide, reaction of the latter with aminoguanidine bicarbonate to produce the cyanoimine intermediate 2-[cyano(2,3-dichlorophenyl)methylene]hydrazinecarboximidamide, and cyclization of this in the presence of aqueous KOH at 80°-reflux.

L10 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1063399 HCAPLUS
DOCUMENT NUMBER: 143:326054
TITLE: Synthesis of 2,3-Dichlorobenzonitrile
AUTHOR(S): Deng, Hong; Liao, Qi; Zhou, Ying
CORPORATE SOURCE: Dept. of Chemistry, Central South Forestry University, Zhuzhou, Hunan Province, 412006, Peop. Rep. China
SOURCE: Jingxi Huagong Zhongjianti (2004), 34(5), 23-24
CODEN: JHZIAR; ISSN: 1009-9212
PUBLISHER: Jingxi Huagong Zhongjianti Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 143:326054

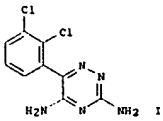
AB 2,3-Dichlorobenzonitrile was the important intermediate for synthesizing 2,3-dichlorobenzoic acid, which is the key intermediate for synthesizing 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine, the specific antiepileptic called Lamotrigine. 2,3-Dichlorobenzonitrile was synthesized from 2,3-dichloroaniline by diazo and Sandmeyer reaction. The yield was over 60%.

L10 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:421470 HCAPLUS
DOCUMENT NUMBER: 141:7119
TITLE: Preparation of crystalline lamotrigine and its monohydrate
INVENTOR(S): Manjunatha, Sulur G.; Kulkarni, Ashok Krishna; Kishore, Charugundia; Bokka, Ravisankar
PATENT ASSIGNEE(S): Jubilant Organosys Limited, India
SOURCE: Brit. UK Pat. Appl., 25 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2395483	A	20040526	GB 2003-15608	20030703
WO 2005003104	A2	20050113	WO 2004-IN186	20040628
WO 2005003104	A3	20050922		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,				

ES, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2003-15608 A 20030703
OTHER SOURCE(S): CASREACT 141:7119
GI



I

AB The invention relates to crystalline lamotrigine (3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine) (I) monohydrate and anhydrous lamotrigine. An improved process for manufacturing these products comprises reacting 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in aqueous mineral acid, optionally together with a water miscible organic solvent, at 30-80° to produce the 2-(2,3-dichlorophenyl)-2-(guanidinylimino)acetonitrile (Schiff base) (II). The Schiff base II is further cyclized in aqueous organic solvent, e.g. alc. to produce pure lamotrigine of a pharmaceutically acceptable quality which on further drying at 45-50° under vacuum yields lamotrigine monohydrate, and/or on further drying at 100-110° yields anhydrous lamotrigine. The lamotrigine monohydrate or anhydrous lamotrigine thereby produced may then be brought into association with a pharmaceutically acceptable carrier for administration to a patient in need thereof.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:390214 HCAPLUS
DOCUMENT NUMBER: 140:391299
TITLE: Process for preparing 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile and a process for its cyclization into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine
INVENTOR(S): Dalmases Barjoan, Pere; Bessa Bellmunt, Jordi
PATENT ASSIGNEE(S): Laboratorios Vita, S.A., Spain
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

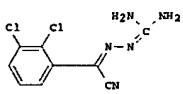
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039767	A1	20040513	WO 2003-IB4763	20031027

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

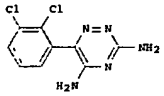
ES 2209639	A1	20040616	ES 2002-2502	20021031
ES 2209639	B1	20050801		
AU 2003272019	A1	20040525	AU 2003-272019	20031027
EP 1556341	A1	20050727	EP 2003-753860	20031027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006052625	A1	20060309	US 2005-532397	20050422
US 7179913	B2	20070220		
NO 2005002574	A	20050527	NO 2005-2574	20050527

PRIORITY APPLN. INFO.: ES 2002-2502 A 20021031
WO 2003-IB4763 W 20031027

OTHER SOURCE(S): CASREACT 140:391299
GI



I



II

AB A method for preparing the intermediate 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile (I; m.p. 180-183°) which comprises the condensation reaction of 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in a non-aqueous medium in the presence of methanesulfonic acid, which produces good I yields and short reaction times. I is cyclized into 3,5-diamino-6-(2,3

-dichlorophenyl)-1,2,4-triazine (II; m.p. 217°) under reflux in an aliph alc. (e.g., ethanol) or alc.-water mixture
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:267313 HCAPLUS
DOCUMENT NUMBER: 140:303705
TITLE: Two-step process for the synthesis of high-purity 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine from 2,3-dichlorobenzoyl cyanide and aminoguanidine dimesylate
INVENTOR(S): Neu, Jozsef; Gizur, Tibor; Toerley, Jozsef; Csabai, Janos; Vegh, Ferenc; Kalvin, Peter; Tarkanyi, Gabor
PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026845	A1	20040401	WO 2003-HU72	20030918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
HU 200203114	A2	20040528	HU 2002-3114	20020920
CA 2498761	A1	20040401	CA 2003-2498761	20030918
AU 2003267676	A1	20040408	AU 2003-267676	20030918
EP 1539720	A1	20050615	EP 2003-748368	20030918
EP 1539720	B1	20061122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 346051	T	20061215	AT 2003-748368	20030918
IN 2005KN00267	A	20060714	IN 2005-KN267	20050224
US 2006178511	A1	20060810	US 2005-528379	20050329
			HU 2002-3114 A	20020920
PRIORITY APPLN. INFO.:			WO 2003-HU72 W	20030918

OTHER SOURCE(S): CASREACT 140:303705
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB High-purity 3,5-diamino-6-(

2,3-dichlorophenyl)-1,2,
4-triazine (I; i.e., lamotrigine) is prepared by the condensation reaction of 2,3-dichlorobenzoyl cyanide (II) with 1-2 mol equivalent of an aminoguanidine salt (e.g., aminoguanidine dimesylate) in 3-6 mol equivalent of methanesulfonic acid, then the obtained adduct (III) is transformed without isolation into the desired product by contacting it with magnesium oxide, followed by crystallization of the product from an appropriate organic solvent (e.g., acetone).
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

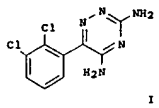
L10 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:159133 HCAPLUS
DOCUMENT NUMBER: 139:316547
TITLE: Transplacental passage of lamotrigine in a human placental perfusion system in vitro and in maternal and cord blood in vivo
AUTHOR(S): Myllynen, Paeivi K.; Pienimaeki, Paeivi K.; Vaehaekangas, Kirsi H.
CORPORATE SOURCE: Department of Pharmacology and Toxicology, University of Oulu, PO Box 5000, Oulu, FIN-90014, Finland
SOURCE: European Journal of Clinical Pharmacology (2003), 58(10), 677-682
CODEN: EJCPAS; ISSN: 0031-6970
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We studied transplacental passage of lamotrigine (3,5-diamino-6-[2,3-dichlorophenyl]-1,2,4-triazine; LTG) using an ex vivo human placental perfusion method and in in vivo samples. Term placentae from healthy mothers without medications were perfused in a recirculating dual perfusion system. LTG (2.5 μg/mL, n = 4; 10 μg/mL, n = 4) and reference compound antipyrine (100 μg/mL) were added into the maternal circulation. The disappearance of drugs from the maternal circulation and appearance into the fetal circulation was followed every 15 min up to 2 h. Drug concns. were analyzed using high-performance liquid chromatog. In addition to human placental perfusions, we analyzed LTG concns. in maternal vein and cord blood samples after delivery from two epileptic mothers receiving LTG therapy during pregnancy. LTG was detectable in the fetal circulation at 15 min in all of the perfusions, indicating rapid transfer. Maternal and fetal concns. reached equilibrium at 60 min with both concns. used. The feto-maternal ratio was 1.26 ± 0.20 with 10 μg/mL LTG and 0.83 ± 0.41 with 2.5 μg/mL LTG at the end of the perfusion. The transfer of LTG from the maternal to the fetal compartment at 120 min was 28.9 ± 10.7% with 2.5 μg/mL LTG and 37.8 ± 3.2% with 10 μg/mL LTG ($p > 0.05$). In the serum samples from epileptic mothers, the cord blood maternal concentration ratio was 1.02 in one pair and 1.55 in the other. LTG crossed the placenta easily and rapidly, indicating that the maternal treatment leads to a considerable fetal exposure.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:76761 HCAPLUS
DOCUMENT NUMBER: 138:137336
TITLE: Method for producing lamotrigine from alpha-oxo-2,3-dichlorophenylacetamidinoaminoguanidino

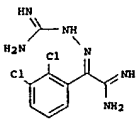
hydrazone by ring closure reaction
INVENTOR(S): Schneider, Geza; Gegoe, Csaba Lehel; Ondi, Levente; Mate, Attila Gergely; Lukacs, Ferenc; Nyerges, Miklos; Garaczi, Sandor
PATENT ASSIGNEE(S): Hela AG, Germany; CF Pharma Gyogyszergyarto Kft.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008393	A1	20030130	WO 2002-EP7433	20020704
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10134980	A1	20030213	DE 2001-10134980	20010717
DE 10134980	C2	20030528		
EP 1311492	A1	20030521	EP 2002-758308	20020704
EP 1311492	B1	20040908		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, BG, CZ, EE				
CA 2417435	C	20040113	CA 2002-2417435	20020704
CA 2417435	A1	20030130		
ES 2224074	T3	20050301	ES 2002-2758308	20020704
US 2003191310	A1	20031009	US 2003-343225	20030515
US 6683182	B2	20040127		

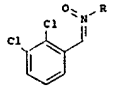
PRIORITY APPLN. INFO.: DE 2001-10134980 A 20010717
WO 2002-EP7433 W 20020704
OTHER SOURCE(S): CASREACT 138:137336; MARPAT 138:137336
GI



I



II



III

AB The invention relates to a method for producing 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine [lamotrigine (I)], or its pharmaceutically acceptable salts, by ring closure reaction from α-oxo-2,3-dichlorophenylacetamidinoaminoguanidino hydrazone (II) or its salts. The preparation of II from N-oxides, III [R = linear, branched or cyclic (un)substituted alkyl, aryl, aralkyl], or their salts, are also described. Thus, I was prepared from 2,3-Cl2C6H3CH:N(O)Ph, via cyanation with NaCN, amination to the acetamidine hydrochloride, reaction with aminoguanine bicarbonate to give II·HCl, treatment with aqueous NaOH to give the free base, which is cyclized to I; cyclization of II·HCl gives I·HCl.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:775487 HCAPLUS
DOCUMENT NUMBER: 138:60875
TITLE: Development of a solid phase extraction protocol for the simultaneous determination of anthracene and its oxidation products in surface waters by reversed-phase HPLC
AUTHOR(S): Papadoyannis, I. N.; Zotou, A.; Samanidou, V. F.
CORPORATE SOURCE: Laboratory of Analytical Chemistry, Department of Chemistry, Aristotle University of Thessaloniki, Thessaloniki, GR-541 24, Greece
SOURCE: Journal of Liquid Chromatography & Related Technologies (2002), 25(17), 2635-2653
CODEN: JLCTFC; ISSN: 1082-6076
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A gradient reversed-phase HPLC (RP-HPLC) method for the simultaneous determination

of anthracene, anthraquinone, and 1-hydroxyanthraquinone, with photodiode array detection at 250 nm, was developed. The separation was achieved on a Kromasil 100 G8 5 μm 250 × 4 mm column, applying a 10-min linear gradient elution starting with 85% methanol and 15% 0.05M ammonium acetate and ending up with 95% of methanol and 5% 0.05M ammonium acetate, at a flow-rate 0.7 mL/min, using 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (lamotrigine) as internal standard Calibration curves were rectilinear for 0.1-3.0 ng anthracene, 0.1-10.0 ng anthraquinone, and 0.5-20.0 ng 1-hydroxyanthraquinone, when 10 μL was injected. The detection limits were 0.05 ng injected on-column for anthracene and anthraquinone and 0.3 ng on-column for 1-hydroxyanthraquinone. The average intra- and inter-day RSDs for injection precision (in terms of peak area) were 1.9% and 3.62%, resp. The method was applied to the anal. of river and lake waters. A protocol, combining solid phase extraction (SPE) with sonication of matrix with sorbent, was developed for enhancement of recovery. The proposed protocol was chosen among other studied, after optimization of each step. Mean recoveries were 50% for anthracene, 71% for anthraquinone, and 105% for 1-hydroxy anthraquinone.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:435163 HCAPLUS
DOCUMENT NUMBER: 133:160143
TITLE: Evidence that DHPG-induced nociception depends on glutamate release from primary afferent C-fibres
AUTHOR(S): Lefebvre, Celeste; Fisher, Kim; Cahill, Catherine M.; Coderre, Terence J.
CORPORATE SOURCE: Pain Mechanisms Laboratory, Clinical Research Institute of Montreal, Montreal, QC, H2W 1R7, Can.
SOURCE: NeuroReport (2000), 11(8), 1631-1635
CODEN: NERPEZ; ISSN: 0959-4965
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors examined whether enhanced glutamate release contributes to the expression of persistent spontaneous nociceptive behaviors (SNBs) in rats induced by intrathecal (i.t.) administration of the selective group I mGluR agonist, (RS)-3,5-dihydroxyphenylglycine ((RS)-DHPG). Pretreatment with drugs that have been shown to inhibit glutamate release, including a group II metabotropic glutamate receptor (mGluR) agonist (2R,4R)-4-aminopyrrolidine-2,4-dicarboxylate ((2R,4R)-APDC), a group III mGluR agonist L-2-amino-4-phosphonobutyrate (L-AP4), or the use-dependent sodium channel blockers 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (lamotrigine) and 2-amino-6-trifluoromethoxybenzothiazole (riluzole), produced dose-dependent redns. in (RS)-DHPG-induced SNBs. The authors have also shown that incubation of rat lumbar spinal cord slices with (RS)-DHPG potentiates 4-aminopyridine-evoked (4-AP) release of glutamate. Furthermore, the authors found that destruction of unmyelinated primary afferent C-fibers by neonatal capsaicin treatment significantly reduced (RS)-DHPG-induced SNBs in adult rats. Together, these results suggest that (RS)-DHPG-induced nociception is dependent on spinal glutamate release, probably from primary afferent C-fibers.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:421116 HCAPLUS
DOCUMENT NUMBER: 133:60362
TITLE: An improved process for preparation of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine
INVENTOR(S): Vyas, Sharad Kumar
PATENT ASSIGNEE(S): India
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035888	A1	20000622	WO 1999-IB1955	19991207
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IN 183150	A1	19990925	IN 1998-CA2171	19981214
CA 2334937	A1	20000622	CA 1999-2334937	19991207
CA 2334937	C	20040921		
AU 2000012924	A	20000703	AU 2000-12924	19991207
EP 1140872	A1	20011010	EP 1999-956293	19991207
EP 1140872	B1	20030917		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 250041	T	20031015	AT 1999-956293	19991207
RU 2231526	C2	20040627	RU 2001-115698	19991207
PRIORITY APPLN. INFO.:			IN 1998-CA2171 A	19981214
			WO 1999-IB1955 W	19991207

AB 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (lamotrigine) (I) useful as antiepileptic drug (no data) is prepared in a 3 step process. Thus, 2,3-dichlorobenzoylchloride was treated with cuprous cyanide in presence of acetonitrile and a solvent to produce 2,3-dichlorobenzoyl cyanide, further with aminoguanidine and cyclized to produce I.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:12098 HCAPLUS
DOCUMENT NUMBER: 132:130210
TITLE: Structure of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine isethionate solvate (lamotrigine isethionate)
AUTHOR(S): Potter, Brian; Palmer, Rex A.; Withnall, Robert;

Leach, Michael J.; Chowdhry, Babur Z.
CORPORATE SOURCE: Department of Crystallography, Birkbeck College, University of London, London, WC1E 7HX, UK
SOURCE: Journal of Chemical Crystallography (1999), 29(6), 701-706
CODEN: JCCYEV; ISSN: 1074-1542
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The crystal and mol. structure of lamotrigine isethionate was determined by direct methods. The compound crystallizes in the tetragonal space group I41/a, with a 19.684(5), c 16.557(5) Å; Z = 16, dc = 1.579; R = 0.0532, Rw = 0.1317 for 2041 reflections. Atomic coordinates are given. The isethionate moiety forms multiple H bonds to the lamotrigine nucleus, three from one isethionate, two from a symmetry related isethionate and a further two from two different symmetry related mols. Protonation of N(2') in the triazine ring, not observed in the native lamotrigine structure is presumably associated with the interaction of the isethionate moiety. Both rings in the lamotrigine moiety are essentially planar, with a dihedral angle of 66.08(7)° compared to 80.70° in native lamotrigine. The connecting bond length C(1)-C(6') 1.493(3) Å also correlates well with values in related compds. (1.480(3) Å) in the native structures.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:682978 HCAPLUS
DOCUMENT NUMBER: 132:98214
TITLE: Detection of the principal synthetic route indicative impurity in lamotrigine
AUTHOR(S): Ashton, D. S.; Ray, A. D.; Valko, K.
CORPORATE SOURCE: School of Pharmacy, University of London, London, UK
SOURCE: International Journal of Pharmaceutics (1999), 189(2), 241-248
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An anal. method has been developed for the detection of trace amts. of the principal synthetic route indicative impurity in lamotrigine (3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine). A sample extract was preconcd. by normal-phase high-performance liquid chromatog. (HPLC) and analyzed by subsequent online reversed-phase HPLC-thermospray mass spectrometry (TSP-MS). During the sample extraction and concentration step, carried out by semipreparative normal-phase chromatog., the preliminary separation of the impurity from the lamotrigine takes place. The organic solvent (dichloroethane-methanol, 90:10, volume/volume) is evaporated from the collected fraction and the material is redissolved in a smaller volume of the reversed-phase mobile phase. The collected fraction is then subjected to reversed-phase HPLC-TSP-MS. The influence of an ultrasonic extraction step has been examined. When the method was applied to lamotrigine tablets, a shake flask partitioning step using 1 mg/mL EDTA in water-dichloroethane was used instead of the ultrasonic extraction. Detection limit and recovery measurements showed that the route indicative impurity formed during the synthesis could be detected in the 50-100 ppb (weight/weight)

range.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:289572 HCAPLUS
DOCUMENT NUMBER: 127:636
TITLE: A calcium antagonistic effect of the new antiepileptic drug lamotrigine
AUTHOR(S): v. Wegerer, J.; Hesslinger, B.; Berger, M.; Walden, J.
CORPORATE SOURCE: Universitaet Freiburg, Abt. Psychiatrie und Psychotherapie, Hauptstr. 5, 79104, Freiburg, Germany
SOURCE: European Neuropsychopharmacology (1997), 7(2), 77-81
CODEN: EURNE8; ISSN: 0924-977X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The new antiepileptic drug lamotrigine (LTG; 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine) has been shown to be effective in the treatment of focal epilepsies with or without secondary generalization. Furthermore, some case reports indicate an efficacy in the treatment of bipolar affective disorders. It has been suggested that the main mechanism of action of LTG is the inhibition of glutamate release through blockade of voltage sensitive sodium channels and stabilization of the neuronal membrane. Since some antidepressant drugs and the antiepileptic substance carbamazepine have calcium antagonistic properties, which may be of significance in the pathophysiol. of epilepsies and affective disorders, the interaction of lamotrigine with carbamazepine and the organic calcium channel blocker verapamil was analyzed in the low Mg2+-induced model epilepsy which has been shown to be suppressed specifically by organic calcium antagonists. Lamotrigine reduced the frequency of occurrence of low-magnesium induced field potentials in CA1 and CA3 areas of the hippocampus slice preparation (guinea pigs) in a dose-dependent manner. The subthreshold concns. which yielded no effect were 1 μmol/L for lamotrigine, 10 μmol/L for carbamazepine and 2 μmol/L for verapamil. Combinations of these subthreshold concns. elicited a reduction in the repetition rate of field potentials. The results indicate that lamotrigine behaves additive with verapamil and carbamazepine what can be due to a common action on the same subtype of calcium channels. It can be assumed that lamotrigine may have besides its action on high-frequency sodium dependent action potentials also effects on calcium channels.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:288924 HCAPLUS
DOCUMENT NUMBER: 126:312094
TITLE: Effects of lamotrigine on brain nitrite and cGMP levels during focal cerebral ischemia in rats
AUTHOR(S): Balkan, S.; Ozben, T.; Balkan, E.; Oguz, N.; Serteser, M.; Gumuslu, S.
CORPORATE SOURCE: Department of Neurology, School of Medicine, Akdeniz University, Antalya, 07070, Turk.
SOURCE: Acta Neurologica Scandinavica (1997), 95(3), 140-146
CODEN: ANRSAS; ISSN: 0001-6314
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal

LANGUAGE: English
AB Glutamate receptor antagonists are protective in animal models of focal cerebral ischemia. Lamotrigine (3,5-diamino-6-[2,3-dichlorophenyl]-1,2,4-triazine) is an anticonvulsant drug that blocks voltage-gated sodium channels and inhibits the ischemia-induced release of glutamate. Expts. in primary neuronal cultures implicate nitric oxide (NO) as a mediator of glutamatergic neurotoxicity acting via N-Methyl-D-Asparate (NMDA) receptors. The effect of glutamate release inhibitor, lamotrigine, upon NO and cGMP production has been examined in focal cerebral ischemia in rats. Focal cerebral ischemia was produced by the permanent occlusion of right middle cerebral artery (MCA) in urethane anesthetized rats. A number of indicators of brain NO production (nitrite, cGMP) were determined in ipsilateral and contralateral cerebral cortex and cerebellum after 0, 10, 60 min of focal cerebral ischemia. The same parameters were measured in rats treated with Lamotrigine (20 mg/kg, i.p.) 30 min before or just after the occlusion of the right MCA.

L10 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:546365 HCAPLUS
DOCUMENT NUMBER: 125:195693
TITLE: Preparation of lamotrigine.
INVENTOR(S): Lee, Grahame Roy
PATENT ASSIGNEE(S): Wellcome Foundation Limited, UK
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9620935	A1	19960711	WO 1995-GB3049	19951229
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9643116	A	19960724	AU 1996-43116	19951229
EP 800521	A1	19971015	EP 1995-941818	19951229
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
HU 77347	A2	19980330	HU 1997-1875	19951229
JP 11507011	T	19990622	JP 1995-520618	19951229
RU 2162081	C2	20010120	RU 1997-112921	19951229
FI 9702720	A	19970827	FI 1997-2720	19970624
US 5925755	A	19990720	US 1997-836152	19970625
PRIORITY APPLN. INFO.:			GB 1994-26448 A	19941230
			WO 1995-GB3049 W	19951229

AB Lamotrigine, 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (I), is prepared by treating 6-(2,3-dichlorophenyl)-5-chloro-3-thiomethyl-1,2,4-triazine (II) with NH3. Thus, II (preparation given) was heated with ethanolic NH3 in a sealed tube at 180° and 280 psi for 72 h to give I.

L10 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:186621 HCAPLUS
DOCUMENT NUMBER: 124:278888
TITLE: Inhibition of morphine withdrawal by lamotrigine: involvement of nitric oxide
AUTHOR(S): Lizasoain, Ignacio; Leza, Juan C.; Cuellar, Beatriz; Moro, Maria A.; Lorenzo, Pedro
CORPORATE SOURCE: Departamento de Farmacologia, Facultad de Medicina, Universidad Complutense de Madrid, Avenida Complutense s/n, Madrid, 28040, Spain
SOURCE: European Journal of Pharmacology (1996), 299(1-3), 41-5
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We studied the effects of lamotrigine [3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine], a new antiepileptic compound, on naloxone-precipitated morphine withdrawal in mice. Pretreatment with lamotrigine (5-100 mg/kg, s.c.) reversed in a dose-dependent way the withdrawal-induced increase in cerebellar Ca2+-dependent nitric oxide (NO) synthase activity and reduced the number of escape jumps and other motor symptoms of abstinence, at doses that did not modify locomotor activity (25-50 mg/kg). Pretreatment with the NMDA receptor antagonist MK-801 [(+)-5-methyl-10,11-dihydroxy-5H-dibenzo[a,d]cyclohepten-5,10-imine; dizocilpine] (0.1-0.3 mg/kg, s.c.) also reversed the increase in cerebellar Ca2+-dependent NO synthase activity. However, although MK-801 reduced the number of escape jumps and other motor symptoms of abstinence, its effects were not clearly dose-dependent. Furthermore, the highest dose of MK-801 tested (0.3 mg/kg) caused an impairment of the locomotor behavior in naive mice. Thus, lamotrigine may represent a new and useful agent for the treatment of opiate abstinence.

L10 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:499316 HCAPLUS
DOCUMENT NUMBER: 123:699
TITLE: Cerebroprotective effect of lamotrigine after focal ischemia in rats
AUTHOR(S): Smith, Stuart E.; Meldrum, Brian S.
CORPORATE SOURCE: Department of Neurology, Institute of Psychiatry, Denmark Hill, SE5 8AF, UK
SOURCE: Stroke (1995), 26(1), 117-22
CODEN: SJCCA7; ISSN: 0039-2499
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Glutamate receptor antagonists are protective in animal models of focal cerebral ischemia. Lamotrigine (3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine) is an anticonvulsant drug that blocks voltage-gated sodium channels and inhibits the ischemia-induced release of glutamate. The cerebroprotective effect of lamotrigine (as the isethionate salt) after middle cerebral artery occlusion was described in rats. Neurol. deficit and infarct volume (visualized by the lack of reduction of 2,3,5-triphenyltetrazolium chloride) 24 h after permanent left middle cerebral artery occlusion were studied in Fischer rats (n=8 per group per dose). Lamotrigine at 20 mg/kg i.v. over

10 min administered immediately after middle cerebral artery occlusion reduced total infarct volume by 31% and cortical infarct volume by 52%. Lamotrigine at 8 mg/kg i.v. over 10 min reduced cortical infarct volume by 38%. Lamotrigine at 50 mg/kg i.v. for 10 min was not cerebroprotective and induced a decrease of 29±15 mm Hg in mean arterial blood pressure (P<.05, n=8). The optimum dose of lamotrigine (20 mg/kg i.v. over 10 min) when administered with a 1-h delay after middle cerebral artery occlusion reduced cortical infarct volume by 41%. Lamotrigine (20 mg/kg i.v. over 10 min) with a 2-h delay after middle cerebral artery occlusion was ineffective. Neurol. deficits after 24 h were improved after immediate treatment with lamotrigine at 20 mg/kg i.v. over 10 min.? The cerebroprotective effect of lamotrigine in rats is limited to a narrow dose range between 8 and 20 mg/kg. Lamotrigine or analogous compds. may be useful when given shortly after the onset of stroke.

L10 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:663729 HCAPLUS
DOCUMENT NUMBER: 121:263729
TITLE: Use of triazine compounds for the treatment of memory and learning disorders
INVENTOR(S): Baxter, Martin George
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9421260	A1	19940929	WO 1994-GB559	19940318
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9462176	A	19941011	AU 1994-62176	19940318
ZA 9401938	A	19950918	ZA 1994-1938	19940318
EP 689439	A1	19960103	EP 1994-909263	19940318
EP 689439	B1	20010124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08507782	T	19960820	JP 1994-520807	19940318
IL 109034	A	19981206	IL 1994-109034	19940318
AT 198831	T	20010215	AT 1994-909263	19940318
ES 2153854	T3	20010316	ES 1994-909263	19940318
PT 689439	T	20010531	PT 1994-909263	19940318
US 5866597	A	19990202	US 1997-900868	19970725
GR 3035528	T3	20010629	GR 2001-400367	20010308
PRIORITY APPLN. INFO.:			GB 1993-5693 A	19930319
			WO 1994-GB559 W	19940318
			US 1996-535140 B1	19960328

AB 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (I) and its pharmaceutically acceptable acid addition salts can be used to treat impaired memory and learning disorders. Therapeutic effects of I were demonstrated in a scopolamine-induced mouse model of memory deficit and compared with those of ondansetron HCl and piracetam. A tablet containing 150 mg I was also formulated.

L10 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:663728 HCAPLUS
DOCUMENT NUMBER: 121:263728
TITLE: Use of triazine compounds as anxiolytics
INVENTOR(S): Critchley, Martyn Alan Edwin
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9421261	A1	19940929	WO 1994-GB560	19940318
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9462177	A	19941011	AU 1994-62177	19940318
ZA 9401939	A	19950918	ZA 1994-1939	19940318
EP 689440	A1	19960103	EP 1994-909264	19940318
EP 689440	B1	20000531		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08507783	T	19960820	JP 1994-520808	19940318
JP 3633618	B2	20050330		
AT 193446	T	20000615	AT 1994-909264	19940318
ES 2147232	T3	20000901	ES 1994-909264	19940318
PT 689440	T	20001031	PT 1994-909264	19940318
US 5658905	A	19970819	US 1995-535139	19950918
GR 3033941	T3	20001130	GR 2000-401626	20000712
PRIORITY APPLN. INFO.:			GB 1993-5692 A	19930319
			WO 1994-GB560 W	19940318

AB 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (I) and its pharmaceutically acceptable acid addition salts can be used to treat anxiety and anxiety disorders. For example, an anxiolytic effect of I-isethionate was demonstrated with Vogel conflict model in rats. A tablet containing 150 mg I was also formulated.

L10 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:124865 HCAPLUS
DOCUMENT NUMBER: 120:124865
TITLE: Use of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine isethionate for the treatment and prevention of dependence on, tolerance to, and sensitization to drugs
INVENTOR(S): Nakamura-Craig, Meire
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9325207	A1	19931223	WO 1993-GB1243	19930611
W: AU, CA, CZ, GB, JP, KR, NO, NZ, PL, RU, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9343452	A	19940104	AU 1993-43452	19930611
AU 688729	B2	19980319		
EP 644763	A1	19950329	EP 1993-913346	19930611
EP 644763	B1	19970122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
GB 2282336	A	19950405	GB 1994-23697	19930611
JP 07507790	T	19950831	JP 1993-501281	19930611
AT 147980	T	19970215	AT 1993-913346	19930611
ES 2097516	T3	19970401	ES 1993-913346	19930611
CZ 284061	B6	19980812	CZ 1994-3128	19930611
IL 105986	A	19981206	IL 1993-105986	19930611
SK 279730	B6	19990211	SK 1994-1534	19930611
HR 930964	B1	20000630	HR 1993-964	19930611
JP 3439211	B2	20030825	JP 1994-501281	19930611
US 5801171	A	19980901	US 1994-347480	19941206
NO 9404790	A	19941209	NO 1994-4790	19941209
PRIORITY APPLN. INFO.:			GB 1992-12495 A	19920612
			GB 1993-8654 A	19930427
			WO 1993-GB1243 A	19930611

AB 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4,-triazine (I) and its pharmaceutically and veterinarily acceptable salts (especially the ethionate) have activity in (a) preventing or reducing dependence on, and (b) preventing or reducing tolerance or reverse tolerance to, a dependence-inducing agent such as an opioid, a central nervous system depressant, a psychostimulant, or nicotine. Thus, I (5 mg/kg orally twice a day during morphine habituation) attenuated the development of morphine tolerance in rats without affecting the analgesic effect of morphine in the tail-flick test.

L10 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:617428 HCAPLUS
DOCUMENT NUMBER: 119:217428
TITLE: Use of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine for the treatment of pain and edema
INVENTOR(S): Nakamura-Craig, Meire; Leach, Michael John
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9316700	A1	19930902	WO 1993-GB341	19930218
W: AU, CA, GB, JP, KR, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

AU 9335092	A	19930913	AU 1993-35092		19930218
AU 684711	B2	19980108			
EP 626851	A1	19941207	EP 1993-904225		19930218
EP 626851	B1	20010822			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 07503968	T	19950427	JP 1993-514628		19930218
JP 3713271	B2	20051109			
IL 104775	A	19970218	IL 1993-104775		19930218
AT 204476	T	20010915	AT 1993-904225		19930218
ES 2162813	T3	20020116	ES 1993-904225		19930218
PT 626851	T	20020228	PT 1993-904225		19930218
CA 2129043	C	20040127	CA 1993-2129043		19930218
GB 2277265	A	19941026	GB 1994-14348		19940715
GB 2277265	B	19960110			
US 5712277	A	19980127	US 1996-680111		19960715
GR 3036958	T3	20020131	GR 2001-401827		20011022
PRIORITY APPLN. INFO.:			GB 1992-3483	A	19920219
			WO 1993-GB341	A	19930218
			US 1994-284497	A1	19940804

AB The title compound (I) is useful in medicaments for the prevention or treatment of pain or edema. A tablet formulation containing I is given. I was tested in rats.

L10 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:126056 HCAPLUS
DOCUMENT NUMBER: 110:126056
TITLE: Structure of lamotrigine methanol solvate: 3 ,5-diamino-6-(2 ,3-dichlorophenyl)-1, 2,4-triazine-methanol, a novel anticonvulsant drug
AUTHOR(S): Janes, Robert W.; Liegarten, John N.; Palmer, Rex A.
CORPORATE SOURCE: Birkbeck Coll., Univ. London, London, WC1E 7HX, UK
SOURCE: Acta Crystallographica, Section C: Crystal Structure Communications (1989), C45(1), 129-32
CODEN: ACSCEE; ISSN: 0108-2701
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The title compound is monoclinic, space group P21/n, with a 15.456(3), b 11.736(2), c 7.300(3) Å, and β 94.417(3)°; Z = 4 for dc = 1.449. The final R = 0.055 for 2444 reflections. Atomic coordinates are given. The Ph and triazine aromatic rings make a dihedral angle of 80.6(9)° with each other. The bond linking the 2 rings is 1.480(3) Å. The structure is stabilized by a network of H bonds involving amino and ring N atoms, one of the Cl atoms, and the MeOH of crystallization

L10 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:112505 HCAPLUS
DOCUMENT NUMBER: 108:112505
TITLE: Preparation of 3,5-diamino -6-(2,3- dichlorophenyl)-1,2, 4-triazine isethionate as an antiepileptic
INVENTOR(S): Sawyer, David Alan; Copp, Frederick Charles
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 5 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 247892	A1	19871202	EP 1987-304776		19870529
EP 247892	B1	19910424			
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
DK 8702759	A	19871201	DK 1987-2759		19870529
DK 166278	B	19930329			
DK 166278	C	19930823			
FI 8702406	A	19871201	FI 1987-2406		19870529
FI 90770	B	19931215			
FI 90770	C	19940325			
AU 8773684	A	19871203	AU 1987-73684		19870529
AU 597982	B2	19900614			
JP 62289570	A	19871216	JP 1987-134772		19870529
JP 07051571	B	19950605			
HU 45978	A2	19880928	HU 1987-2487		19870529
HU 196769	B	19890130			
ZA 8703896	A	19890125	ZA 1987-3896		19870529
US 4847249	A	19890711	US 1987-56136		19870529
AT 62902	T	19910515	AT 1987-304776		19870529
CA 1286670	C	19910723	CA 1987-538395		19870529
IL 82710	A	19920115	IL 1987-82710		19870529
PRIORITY APPLN. INFO.:			GB 1986-13183	A	19860530
			EP 1987-304776	A	19870529

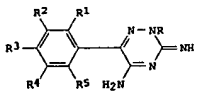
AB The title compound (I.isethionate), useful as an anticonvulsant (no data), was prepared by reaction of I with 2-hydroxyethanesulfonic acid (II) or by reaction of I salts with the anion of II. A 1.0 M solution of Na isethionate in H2O was passed through a column of IR 120 (H) ion exchange resin. I (preparation given) was added to the resulting II and the solution was filtered and evaporated Recrystn. from industrial methylated spirit gave 72% I.isethionate.

L10 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:542021 HCAPLUS
DOCUMENT NUMBER: 103:142021
TITLE: Triazine compounds having cardiovascular activity
INVENTOR(S): Allan, Geoffrey; Miller, Alastair Ainslie; Sawyer, David Alan
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 142306	A2	19850522	EP 1984-307374	19841026
EP 142306	A3	19861120		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4649139	A	19870310	US 1984-663682	19841022
DK 8405121	A	19850428	DK 1984-5121	19841026
FI 8404212	A	19850428	FI 1984-4212	19841026
AU 8434758	A	19850509	AU 1984-34758	19841026

AU 564667	B2	19870820			
JP 60109577	A	19850615	JP 1984-225636		19841026
DD 224033	A5	19850626	DD 1984-268757		19841026
HU 36102	A2	19850828	HU 1984-4003		19841026
HU 191566	B	19870330			
ES 537104	A1	19860416	ES 1984-537104		19841026
ZA 8408388	A	19860625	ZA 1984-8388		19841026
SU 1371500	A3	19880130	SU 1984-3805251		19841026
IL 73332	A	19880630	IL 1984-73332		19841026
PL 144899	B1	19880730	PL 1984-250213		19841026
CA 1261328	A1	19890926	CA 1984-466473		19841026
PRIORITY APPLN. INFO.:			GB 1983-28757	A	19831027
OTHER SOURCE(S):		MARPAT 103:142021			

GI



I

AB Tautomeric iminotriazinamines I [R = (un)substituted C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, C3-10 cycloalkyl; R1-R5 = H, halogen, alkenyloxy, acyl, acyloxy, cyano, NO2, aryl, alkylthio, (un)substituted alkyl, alkenyl, alkynyl, alkoxy, amino; R1R2, R2R3, R3R4, R4R5 = CH:CHCH:CH] were prepared Thus, 3,5-diamino-6-(2,3-dichlorophenyl)-1,2, 4-triazine was alkylated with Me2CHI to give I-HI (R = Me2CH, R1 = R2 = Cl; R3-R5 = H) which was converted to the mesylate salt (II) (12% overall yield). II at 1 mg/kg i.v. to rats increased the amount of aconitine required to elicit ventricular arrhythmias by 490% compared with 84% for 1 mg/kg verapamil.

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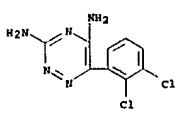
L11 1 84057-84-1/RN

=> d scan

L11 1 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-
MF C9 H7 Cl2 N5
CI COM



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CA SUBSCRIBER PRICE	0.00	-40.56

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(FILE 'HOME' ENTERED AT 16:55:13 ON 04 APR 2007)

FILE 'REGISTRY' ENTERED AT 16:55:37 ON 04 APR 2007
L1 STRUCTURE UPLOADED
L2 3 S L1 SSS SAM
L3 128 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 16:56:47 ON 04 APR 2007
L4 25 S L3/P
E US20050238724/PN,PRN,AN
L5 0 S E3/RN
L6 1 S E3

FILE 'REGISTRY' ENTERED AT 16:58:38 ON 04 APR 2007
L7 0 S L6

FILE 'HCAPLUS' ENTERED AT 17:00:04 ON 04 APR 2007
E LAMOTRIGINE+ALL/CT
S LAMOTRIGINE/CN

FILE 'REGISTRY' ENTERED AT 17:00:26 ON 04 APR 2007
L8 1 S LAMOTRIGINE/CN

FILE 'HCAPLUS' ENTERED AT 17:00:27 ON 04 APR 2007
L9 1265 S L8
L10 27 S "3,5-DIAMINO-6-(2,3-DICHLOROPHENYL)-1,2,4-TRIAZINE"

FILE 'REGISTRY' ENTERED AT 17:02:26 ON 04 APR 2007
L11 1 S 84057-84-1/RN

FILE 'HCAPLUS' ENTERED AT 17:02:48 ON 04 APR 2007

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L12 1265 L11

=> s l10 or l12 and particle or granule
740429 PARTICLE
814603 PARTICLES
1234571 PARTICLE
(PARTICLE OR PARTICLES)
49055 GRANULE

86594 GRANULES
111146 GRANULE
(GRANULE OR GRANULES)
L13 111187 L10 OR L12 AND PARTICLE OR GRANULE

=> s l12 near particle
MISSING OPERATOR L12 NEAR
The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

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740429 PARTICLE
814603 PARTICLES
1234571 PARTICLE
(PARTICLE OR PARTICLES)
L14 0 L12 (A) PARTICLE

=> s l12 (w) particle
740429 PARTICLE
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(PARTICLE OR PARTICLES)
L15 0 L12 (W) PARTICLE

=> s l12 and cns
38387 CNS
L16 46 L12 AND CNS

=> d l16 1-46 ibib abs

L16 ANSWER 1 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:259533 HCAPLUS
DOCUMENT NUMBER: 146:302318
TITLE: 5-HT1B antagonist composition for treating CNS conditions
INVENTOR(S): Harrison, Wilma Marcia; Sobolov-Jaynes, Susan Beth; Foerster, Robert Sterling, Jr.; Van Beek, Jeroen Bernard
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 46pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007026219	A2	20070308	WO 2006-IB2364	20060821

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

JP 2007063277	A	20070315	JP 2006-233101	20060830

PRIORITY APPLN. INFO.: US 2005-712954P P 20050831
AB The present invention relates to pharmaceutical compns. comprising 5-HT1B antagonists in combination with noradrenaline re-uptake inhibitor (NRI) or serotonin noradrenaline reuptake inhibitor (SNRI) and optionally a pharmaceutically acceptable carrier, and to their medicinal use in treating or preventing CNS conditions such as depression, anxiety, cognitions, ADHD, and comorbid indications.

L16 ANSWER 2 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:226913 HCAPLUS
DOCUMENT NUMBER: 146:280994
TITLE: Reducing myocardial damage and the incidence of arrhythmia arising from loss, reduction or interruption in coronary blood flow
INVENTOR(S): Weiss, Steven Michael
PATENT ASSIGNEE(S): Australia
SOURCE: PCT Int. Appl., 47pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007022568	A1	20070301	WO 2006-AU1207	20060824

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: AU 2005-904615 A 20050825
AB A method and composition is disclosed for reducing the extent of cardiac arrhythmias, both resulting from loss, decrease or interruption to the blood supply such as may happen during a heart attack or during cardiac surgery, in mammals. In particular, the present invention relates to a method of limiting or preventing cardiac cell damage and/or death, and limiting or preventing lethal or non-lethal cardiac arrhythmias, in a human, by administering to the cardiac cells a compound which selectively blocks or partially blocks persistent sodium currents and/or persistent sodium channels of cardiac cells. The composition involves any physiol. acceptable chemical or pharmaceutical composition comprising as its active ingredient a cardiac persistent sodium current and/or persistent sodium channel blocker.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:136851 HCAPLUS

TITLE: Recent advances in anti-epileptic drugs
AUTHOR(S): Khan, S. A.; Lamba, H. S.; Rathour, Arvind; Budhwaar, Vikas; Pahwa, Rakesh; Manjusha
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Jamia Hamdard, New Delhi, 110 062, India
SOURCE: Asian Journal of Chemistry (2007), 19(2), 823-835
CODEN: AJCHEW; ISSN: 0970-7077
PUBLISHER: Asian Journal of Chemistry
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Epilepsies are a group of disorders of the CNS characterized by paroxysmal cerebral dysrhythmia, manifesting as brief episodes (seizures) of loss or disturbance of consciousness, with or without characteristic body movements (convulsions), sensory or psychiatric phenomena. Epilepsy has a focal origin in the brain, manifestations depend on the site of the focus, regions into which the discharges spread. Some newer anti-epileptic drugs have recently been developed. They have some advantages over the older drugs. These newer drugs may control seizures more effectively. They are effective in complex partial and secondary generalized seizures. These are felbamate, vigabatrin, gabapetin, clobazam, lamotrigine, oxcarbazepine, tiagabine, topiramate, fosphenytoin, and zonisamide.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

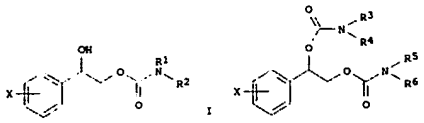
L16 ANSWER 4 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:61845 HCAPLUS
DOCUMENT NUMBER: 146:135588
TITLE: Neuroprotective carbamate derivs. for treatment of neurodegenerative disorders
INVENTOR(S): Zhao, Boyu; Tywman, Roy E.
PATENT ASSIGNEE(S): Janssen Pharmaceutica, N.V., Belg.
SOURCE: PCT Int. Appl., 83pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007008562	A2	20070118	WO 2006-US26291	20060707

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2007021500	A1	20070125	US 2006-481601	20060706

PRIORITY APPLN. INFO.: US 2005-698403P P 20050712
OTHER SOURCE(S): MARPAT 146:135588
GI



I

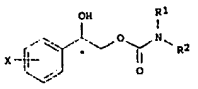
II

AB This invention is directed to methods for providing neuroprotection comprising administering to a subject in need thereof a therapeutically effective amount of a compound selected from Formula (I) and Formula (II), where Ph is substituted at X with 1-5 halo atoms selected from F, C, B or I and R1-R6 = (un)substituted C1-C4 alkyl or pharmaceutical acceptable salts or esters thereof. Carbamate derivative decreased infarct volume following reperfusion in a rat model of transient cerebral ischemia arising from middle cerebral artery occlusion.

L16 ANSWER 5 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:61839 HCAPLUS
DOCUMENT NUMBER: 146:156257
TITLE: Carbamate compounds for treating epileptogenesis
INVENTOR(S): Tvyman, Roy E.; Zhao, Boyu
PATENT ASSIGNEE(S): Janssen Pharmaceutica, N.V, Belg.
SOURCE: PCT Int. Appl., 82pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007008551	A2	20070118	WO 2006-US26277	20060707
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2007021501	A1	20070125	US 2006-481626	20060706

PRIORITY APPLN. INFO.: US 2005-698625P P 20050712
OTHER SOURCE(S): MARPAT 146:156257
GI



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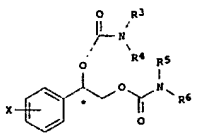


II

AB The invention is directed to methods for preventing, treating, reversing, inhibiting, or arresting epileptogenesis in a subject comprising administering to the subject in need thereof a therapeutically effective amount of a compound selected from the group consisting of Formula (I) and Formula (II),, where Ph is substituted at X with F, Cl, Br, or I; and R1-R6 = (un)substituted C1C4 alkyl or a pharmaceutically acceptable salt or ester thereof. A carbamate compound demonstrated anti-epileptogenic effects in rat model of spontaneous seizures.

L16 ANSWER 6 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1207236 HCAPLUS
DOCUMENT NUMBER: 145:495703
TITLE: Methods and compositions for the treatment of CNS-related conditions
INVENTOR(S): Went, Gregory T.; Pultz, Timothy J.
PATENT ASSIGNEE(S): Neuromolecular Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 58pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006121560	A2	20061116	WO 2006-US13506	20060406
WO 2006121560	A3	20070315		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

KG, KZ, MD, RU, TJ, TM

US 2006142398	A1	20060629	US 2005-285905	20051122
PRIORITY APPLN. INFO.:			US 2005-669290P	P 20050406
			US 2005-285905	A 20051122
			US 2004-630885P	P 20041123
			US 2004-635365P	P 20041210
			US 2005-701857P	P 20050722

AB In general, the present invention provides methods and compns. for treating and preventing CNS-related conditions, such as neurodegenerative conditions (e.g., Alzheimer's disease and Parkinson's disease) and pain, by administering to a subject in need thereof a combination that includes an N-Methyl-D-Aspartate receptor (NMDAr) antagonist and a second agent such as acetylcholinesterase inhibitor (ACheI).

L16 ANSWER 7 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1173916 HCAPLUS
DOCUMENT NUMBER: 145:477933
TITLE: Methods and compositions for the treatment of CNS-related conditions
INVENTOR(S): Went, Gregory T.; Pultz, Timothy J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 29pp., Cont.-in-part of U.S. Ser. No. 285,905.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006252788	A1	20061109	US 2006-399879	20060406
US 2006142398	A1	20060629	US 2005-285905	20051122
PRIORITY APPLN. INFO.:			US 2005-669290P	P 20050406
			US 2005-285905	A2 20051122
			US 2004-630885P	P 20041123
			US 2004-635365P	P 20041210
			US 2005-701857P	P 20050722

AB The present invention provides novel methods and compns. for the treatment and prevention of CNS-related conditions. One of the CNS-related conditions treated by the methods and compns. of the invention is Alzheimer's disease.

L16 ANSWER 8 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:804735 HCAPLUS
DOCUMENT NUMBER: 146:243958
TITLE: Quantitative EEG effects of carbamazepine, oxcarbazepine, valproate, lamotrigine, and possible clinical relevance of the findings
AUTHOR(S): Clemens, Bela; Menes, Andrea; Piros, Palma; Bessenyei, Monika; Altmann, Anna; Jerney, Judit; Kollar, Katalin; Rosdy, Beata; Rozsavoelgyi, Margit; Steinecker, Katalin; Hollody, Katalin
CORPORATE SOURCE: Epilepsy Center, Department of Neurology, Kenezy Gyula Memorial Hospital, Debrecen, 4031, Hung.
SOURCE: Epilepsy Research (2006), 70(2-3), 190-199
CODEN: EPIRE8; ISSN: 0920-1211
PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Quant. EEG (QEEG) effects of therapeutic doses of carbamazepine (CBZ), oxcarbazepine (OXC), valproate (VA) and lamotrigine (LA) monotherapy were investigated in patients with beginning epilepsy. Baseline waking EEG (EEG1) was recorded in the untreated state, the second EEG (EEG2) was done after 8 wk of reaching the therapeutic dose. Left occipital data were used for anal. QEEG target parameters were absolute band-power (delta: AD, theta: AT, alpha: AA, beta: AB), and alpha mean frequency (AMF). Group effects (untreated vs. treated condition in the CBZ, VA, OXC, LA groups) were computed for each target parameter. One group with benign rolandic epilepsy remained untreated for clin. reasons and served to estimate the QEEG test-retest differences. In addition, the individual QEEG response to each drug was calculated as (EEG2 - EEG1). Results: statistically significant ($p < 0.05$) group differences indicated the QEEG domain systematically affected by the drugs. CBZ caused AT increase and AMF decrease. OXC caused AMF decrease. VA and LA did not decrease AMF (LA even increased it), but reduced broad-band power. Individual power and AMF changes showed considerable variability in each group. >0.5 Hz AMF decrease (that was reported to predict cognitive impairment in prior studies) occurred in 10/41 patients in the CBZ group but never in the OXC, VA, LA groups. The results may be utilized in planning further studies addressing the relationship between antiepileptic drugs and their CNS effects. In addition, the relationship of AED-related cognitive impairment and AMF changes was discussed.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:740619 HCAPLUS
DOCUMENT NUMBER: 145:159852
TITLE: Method for treating borderline personality disorder and self-injurious behavior with glutamate-modulating agents
INVENTOR(S): Feuerstein, Seth; Coric, Vladimir
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 9 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006167068	A1	20060727	US 2006-339881	20060126
PRIORITY APPLN. INFO.:			US 2005-647535P	P 20050126

AB Glutamate-modulating agents are useful for treating borderline personality disorder and self-injurious behavior. Methods for treating borderline personality and self-injurious behavior are provided which involve administering a glutamate-modulating agent to a patient. The invention also includes combination methods of treatment in which a glutamate-modulating agent is administered with one or more other CNS active agents. Packaged pharmaceutical compns. containing a glutamate-modulating agent and one or more other CNS agent are also provided, as are packaged pharmaceutical formulations containing a glutamate-modulating agent and instructions for using the glutamate-modulating agent for treating borderline personality disorder or self-mutilating behavior.

L16 ANSWER 10 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:493860 HCAPLUS
DOCUMENT NUMBER: 144:481072
TITLE: Methods and compositions for treating pain
INVENTOR(S): Robbins, Wendye
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 61 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006111307	A1	20060525	US 2005-281791	20051116
US 2006111308	A1	20060525	US 2005-281984	20051116
WO 2006055672	A2	20060526	WO 2005-US41608	20051116
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
GB 2423928	A	20060913	GB 2006-6028	20051116
PRIORITY APPLN. INFO.:			US 2004-628646P	P 20041116
			WO 2005-US41608	W 20051116

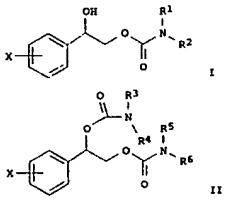
AB Methods and compns. are described for the modulation of central nervous system and/or fetal effects of substances. Methods and compns. are described for the modulation of efflux transporter activity to increase the efflux of drugs and other compds. out of a physiol. compartment and into an external environment. In particular, the methods and compns. disclosed herein provide for the increase of efflux transporter activity at blood-brain, blood-CSF and placental-maternal barriers to increase the efflux of drugs and other compds. from physiol. compartments, including central nervous system and fetal compartments.

L16 ANSWER 11 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:383992 HCAPLUS
DOCUMENT NUMBER: 144:404414
TITLE: Carbamate compounds for use in treating neurodegenerative disorders
INVENTOR(S): Twyman, Roy E.; Zhao, Boyu
PATENT ASSIGNEE(S): Janssen Pharmaceutica, N.V., Belg.
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2006044472	A1	20060427	WO 2005-US36695	20051014
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:			US 2004-619402P	P 20041015
			US 2005-698403P	P 20050712

OTHER SOURCE(S): MARPAT 144:404414
GI



I

II

AB The invention discloses methods for providing neuroprotection, comprising administering to a subject in need thereof a therapeutically effective amount of a compound I or II [Ph is substituted at X with 1-5 halo atoms selected from F, Cl, Br, I; R1-R6 = H, (un)substituted C1-C4 alkyl], or a pharmaceutically acceptable salt or ester thereof.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 12 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:333530 HCAPLUS
DOCUMENT NUMBER: 144:324867
TITLE: Methods of treating epileptogenesis and epilepsy
INVENTOR(S): Choi, Yong Moon; Gordon, Robert; Novak, Gerald P.; Plata-Salaman, Carlos R.; Twyman, Roy E.; White, H. Steve; Zhao, Boyu
PATENT ASSIGNEE(S): Janssen Pharmaceutica, N.V., Belg.
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

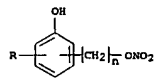
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006033947	A2	20060330	WO 2005-US32861	20050915
WO 2006033947	A3	20060629		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006194873	A1	20060831	US 2005-227247	20050915
PRIORITY APPLN. INFO.:			US 2004-610276P	P 20040916
			US 2005-698625P	P 20050712
			US 2005-707242P	P 20050811

OTHER SOURCE(S): MARPAT 144:324867
AB This invention is directed to methods for preventing, treating, reversing, inhibiting or arresting epilepsy and epileptogenesis in a subject comprising administering to the subject in need thereof a therapeutically effective amount of a compound selected from the group consisting of Formula (I) and Formula (II), or a pharmaceutically acceptable salt or ester thereof,: Formula (I) Formula (II) wherein Ph is substituted at X with one to five halogen atoms selected from the group consisting of fluorine, chlorine, bromine and iodine; and, R1, R2, R3, R4, R5 and R6 are independently selected from the group consisting of hydrogen and C1-C4 alkyl; wherein C1-C4 alkyl is optionally substituted with Ph (wherein Ph is optionally substituted with substituents independently selected from the group consisting of halogen, C1-C4 alkyl, C1-C4 alkoxy, amino, nitro and cyano).

L16 ANSWER 13 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:149768 HCAPLUS
DOCUMENT NUMBER: 144:232798
TITLE: Preparation of nitroxyalkyl derivatives of phenol for treating inflammatory, cardiovascular and peripheral vascular diseases
INVENTOR(S): Ongini, Ennio; Impagnatiello, Francesco
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006015930	A1	20060216	WO 2005-EP53500	20050720
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2004-599857P P 20040810
OTHER SOURCE(S): MARPAT 144:232798
GI



I

AB The title compds. I [n = 1-20; R = H, halo, a linear or branched (C1-C10)alkoxy, OH, CF3, NHR' (wherein R' = H or a linear or branched (C1-C10)alkyl); or a salt thereof], useful for treating inflammatory disease states or disorders, cardiovascular and/or peripheral vascular diseases, were prepared E.g., a benzenemethanol, 3-hydroxy-α-nitrate (II) was prepared from com. available 3-[(hydroxy)methyl]phenol using 2-step process. Effects of II on inflammatory markers were tested. For example, the compound II applied alone or in combination with ASA inhibited LPS/INFγ-induced nitrites accumulation with similar potency as that estimated for NCX 4016 (EC50 = 58 μM and 57 μM, resp. for compound II alone and in combination with ASA). The pharmaceutical compns. comprising the compound II alone or in combination with other therapeutic agents are disclosed.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 14 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:149494 HCAPLUS
DOCUMENT NUMBER: 144:205795
TITLE: Preventing pathological increases in the rate of nerve cell suicide in immature nervous systems
INVENTOR(S): Olney, John W.
PATENT ASSIGNEE(S): Olney, John, W., USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006017524	A2	20060216	WO 2005-US27460	20050802
WO 2006017524	A3	20060831		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,				

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-598390P P 20040802

AB Methods and compds. are disclosed for reducing brain damage in fetuses, neonates, and young infants, caused by surgical anesthetics. During critical periods of synapse formation and network development in the brain, CNS neurons that do not appear to be keeping pace with certain synchronized development and connection processes are regarded as surplus, and are destroyed by a programmed cell suicide process called apoptosis. As a result, if surgical anesthetics block neuronal responses and activities that normally would indicate that a certain CNS neuron is indeed active and involved in a network and should be preserved, such anesthesia can induce apoptotic death, in the unresponsive anesthetized neurons. That process, which can cause permanent brain damage, can be minimized by manipulating certain signaling pathways that affect the balance between apoptosis-promoting proteins (e.g., Bax and Bak) and apoptosis-blocking proteins (e.g., Bcl-2 and Bcl-xL). Agents that have been tested and shown to reduce anesthesia-induced brain damage in neonatal animals include xenon (which promotes ERK MAPKinase activity), and muscarinic cholinergic agonists (which can promote ERK MAPKinase, PKA, PKC, and/or PI3K/AKT activity). Other candidate agents with similar activities include lithium, beta-1 adrenergic antagonists, and beta-2 adrenergic agonists. Such agents must intervene in the "upstream" part of the apoptosis cascade, before mitochondrial membranes become permeable and begin to release "cytochrome c" messenger mols.

L16 ANSWER 15 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:962027 HCAPLUS
DOCUMENT NUMBER: 143:235530
TITLE: Methods and compositions for the treatment of epilepsy, seizure disorders, and other CNS disorders
INVENTOR(S): Went, Gregory; Fultz, Timothy J.; Meyerson, Lawrence
PATENT ASSIGNEE(S): Neuromolecular, Inc., USA; Neuromolecular Pharmaceuticals, Inc.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005079773	A2	20050901	WO 2005-US4819	20050214
WO 2005079773	A3	20051027		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2005215767	A1	20050901	AU 2005-215767	20050214
CA 2556214	A1	20050901	CA 2005-2556214	20050214
EP 1727538	A2	20061206	EP 2005-732251	20050214
R: AT, BE, BG, CH, CY, CZ, DE, DK, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 1929830	A	20070314	CN 2005-80007919	20050214

PRIORITY APPLN. INFO.: US 2004-544839P P 20040213
US 2004-603903P P 20040824
US 2004-635786P P 20041213
WO 2005-US4819 W 20050214

AB The present invention relates to compns. comprising an NMDA receptor antagonists and an anti-epileptic drug for the treatment of CNS -related disorders. For example, tablets were formulated containing memantine 10, topiramate 30, dicalcium phosphate dihydrate 26.6, microcryst. cellulose 26.6, Na starch glycolate 1.2, Mg stearate 0.6, Eudragit RS30D 4.76, talc 3.3, and tri-Et citrate 0.95 mg per tablet.

L16 ANSWER 16 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:673292 HCAPLUS
DOCUMENT NUMBER: 143:172866
TITLE: Preparation of isothiazole dioxides as CXC- and CC-chemokine receptor ligands
INVENTOR(S): Taveras, Arthur G.; Zheng, Junying; Biju, Purakkattle J.; Yu, Younong; Chao, Jianhua; Fine, Jay; Lundell, Daniel; Priestley, Tony; Reggiani, Angelo; Merritt, J. Robert; Baldwin, John J.; Lai, Gaifa; Wu, Minglang
PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia Drug Discovery, Inc.
SOURCE: PCT Int. Appl., 427 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005068460	A1	20050728	WO 2004-US42720	20041220

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2550540	A1	20050728	CA 2004-2550540	20041220
US 2006025453	A1	20060202	US 2004-17505	20041220
EP 1697354	A1	20060906	EP 2004-814856	20041220

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU

CN 1918156	A	20070221	CN 2004-80041794	20041220

PRIORITY APPLN. INFO.: US 2003-531693P P 20031222
WO 2004-US42720 W 20041220

OTHER SOURCE(S): MARPAT 143:172866
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed are novel compds. I [D, E = N, CR50; provided that D and E are not the same (one is N and the other is CR50); R50 = H, CF3, CN, etc.; A = (hetero)aryl, (hetero)arylalkyl; B = (hetero)aryl] and the pharmaceutically acceptable salts and solvates thereof. Also disclosed is a method of treating a chemokine mediated diseases, such as, cancer, angiogenesis, angiogenic ocular diseases, pulmonary diseases, multiple sclerosis, rheumatoid arthritis, osteoarthritis, stroke and cardiac reperfusion injury, pain (e.g., acute pain, acute and chronic inflammatory pain, and neuropathic pain) using a compound I. Although the methods of preparation are not claimed, hundreds of example prepns. and/or characterization data are included. For example, II was prepared in 68% yield from the isothiazoledioxide III and the amine IV.pTSA (preparation of reactants given). Antagonist activities of some examples of I towards CXCR1, CXCR2 and CCR7 are given.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 17 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:638859 HCAPLUS
DOCUMENT NUMBER: 143:153384
TITLE: Preparation of diaminothiadiazoles as CXC- and CC-chemokine receptor ligands
INVENTOR(S): Biju, Purakkattle J.; Taveras, Arthur G.; Yu, Younong; Zheng, Junying; Chao, Jianhua; Aki, Cynthia J.; Fine, Jay; Lundell, Daniel; Priestley, Tony; Reggiani, Angelo; Merritt, J. Robert; Baldwin, John J.
PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia Drug Discovery, Inc.
SOURCE: PCT Int. Appl., 593 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005066147	A1	20050721	WO 2004-US42060	20041216

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

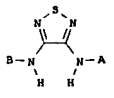
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,

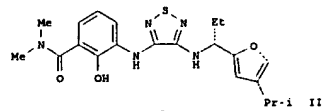
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

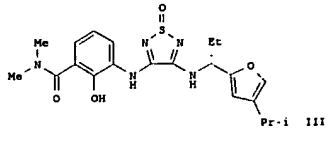
CA 2550189	A1	20050721	CA 2004-2550189	20041216
EP 1694659	A1	20060830	EP 2004-814266	20041216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
US 2006223864	A1	20061005	US 2004-13753	20041216
CN 1918138	A	20070221	CN 2004-80041695	20041216

PRIORITY APPLN. INFO.: US 2003-531311P P 20031219
US 2003-531713P P 20031222
WO 2004-US42060 W 20041216

OTHER SOURCE(S): MARPAT 143:153384
GI







AB Disclosed are diaminothiadiazoles I [A = (hetero)aryl, (hetero)arylmethyl (substituted at CH2), etc.; B = (hetero)aryl] and the pharmaceutically acceptable salts and solvates thereof. Also disclosed is a method of treating a chemokine mediated diseases, such as, cancer, angiogenesis, angiogenic ocular diseases, pulmonary diseases, multiple sclerosis, rheumatoid arthritis, osteoarthritis, stroke and ischemia reperfusion injury, acute pain, acute and chronic inflammatory pain, and neuropathic pain using I. Although the methods of preparation are not claimed, hundreds of example prepns. and/or characterization data are included. For example, II was prepared in 43% yield from its monooxide III (preparation given). Antagonist activities of some examples of I towards CXCR1, CXCR2 and CCR7

are given.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 18 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:364521 HCAPLUS
DOCUMENT NUMBER: 143:126473
TITLE: Valproic acid, but not lamotrigine, suppresses seizure-induced c-fos and c-Jun mRNA expression
AUTHOR(S): Szot, Patricia; White, Sylvia S.; Shen, Danny D.; Anderson, Gail D.
CORPORATE SOURCE: Mental Illness Research Education and Clinical Center (MIRECC), VA Puget Sound Health Care System, Seattle, WA, 98108, USA
SOURCE: Molecular Brain Research (2005), 135(1-2), 285-289
CODEN: MBREE4; ISSN: 0169-328X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Seizure-induced activity was shown to increase the expression of immediate early genes (IEGs) c-fos and c-Jun in the CNS. Antiepileptic drugs (AEDs) can suppress the induction of a seizure, but it is unknown if AEDs affect the expression of seizure-induced IEGs. The authors found that valproic acid (VPA), but not lamotrigine (LTG), was capable of suppressing seizure-induced c-fos and c-Jun mRNA expression in rats despite a similar anticonvulsant effect. LTG in some regions of the CNS enhanced seizure-induced IEG expression. These studies indicate that the older AED (VPA), as compared to the newer AED (LTG), can suppress seizure-induced IEG expression. The consequence of this suppression of IEGs following a generalized seizure may be viewed either as a neuroprotective or detrimental effect upon the brain.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 19 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:288391 HCAPLUS
DOCUMENT NUMBER: 143:71550
TITLE: Adverse reactions of topiramate and lamotrigine in children
AUTHOR(S): Shechter, Tamar; Shorer, Zamir; Kramer, Uri; Lerman-Sagie, Tally; Ronen, Elisheva; Rotem, Rimona; Gorodischer, Rafael
CORPORATE SOURCE: Pharmacy Services, Soroka Medical Center, Be'er Sheva, Israel
SOURCE: Pharmacoepidemiology and Drug Safety (2005), 14(3), 187-192
CODEN: PDSAEA; ISSN: 1053-8569
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: To review the adverse drug reactions (ADRs) of Topiramate and Lamotrigine among children in Israel, and to compare the two drugs, based on their side effect profile and tolerability among this population. Methods: We performed a cross-sectional study. Four pediatric neurologists from three different tertiary medical centers in Israel documented all cases of children from birth to the age 18 years, treated with Topiramate and/or Lamotrigine in their resp. outpatient clinics and hospital wards. All present ADRs and their characteristics were recorded. Results: Reports on 45 and 65 children treated with Topiramate and

Lamotrigine resp., were received. Half of the children treated with Topiramate suffered from one or more ADRs, as opposed to one-third of the children treated with Lamotrigine ($p = 0.03$). Most reactions were considered mild to moderate. There were no deaths or hospitalizations, but the drug had to be discontinued in about 10% of the patients due to ADRs. Most Topiramate and Lamotrigine ADRs appeared early in the treatment and were more frequent when Topiramate was an add-on vs. a monotherapy drug. Most ADRs of both Topiramate and Lamotrigine were related to the central nervous system; while poor appetite, drowsiness, speech difficulties and weight loss were observed only with Topiramate, and rash and headaches only with Lamotrigine. Nervousness and seizure aggravation were more frequent ADRs of Topiramate whereas sleep disturbances were observed more in children treated with Lamotrigine. Conclusion: Results of this study indicate that Lamotrigine causes ADRs less frequently than Topiramate; however both medications are generally well tolerated. Topiramate and Lamotrigine differ in their central nervous system side effect profile.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 20 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:53346 HCAPLUS
DOCUMENT NUMBER: 142:290582
TITLE: Relationship between exposure and nonspecific binding of thirty-three central nervous system drugs in mice
AUTHOR(S): Maurer, Tristan S.; DeBartolo, Demetria B.; Tess, David A.; Scott, Dennis O.
CORPORATE SOURCE: Pharmacokinetics, Pharmacodynamics and Drug Metabolism, Pfizer Global Research and Development, Groton Laboratories, Groton, CT, USA
SOURCE: Drug Metabolism and Disposition (2005), 33(1), 175-181
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Unbound fractions in mouse brain and plasma were determined for 31 structurally diverse central nervous system (CNS) drugs and two active metabolites. Three comparisons were made between in vitro binding and in vivo exposure data, namely: (1) mouse brain-to-plasma exposure vs. unbound plasma-to-unbound brain fraction ratio (fuplasma/fubrain), (2) cerebrospinal fluid-to-brain exposure vs. unbound brain fraction (fubrain), and (3) cerebrospinal fluid-to-plasma exposure vs. unbound plasma fraction (fuplasma). Unbound fraction data were within 3-fold of in vivo exposure ratios for the majority of the drugs examined (i.e., 22 of 33), indicating a predominately free equilibrium across the blood-brain and blood-CSF barriers. Some degree of distributional impairment at either the blood-CSF or the blood-brain barrier was indicated for 8 of the 11 remaining drugs (i.e., carbamazepine, midazolam, phenytoin, sulpiride, thiopental, risperidone, 9-hydroxyrisperidone, and zolpidem). In several cases, the indicated distributional impairment is consistent with other independent literature reports for these drugs. Through the use of this approach, it appears that most CNS-active agents freely equilibrate across the blood-brain and blood-CSF barriers such that unbound drug concns. in brain approx. those in the plasma. However, these results also support the intuitive concept that distributional impairment does not necessarily preclude CNS activity.
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 21 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:53345 HCAPLUS
DOCUMENT NUMBER: 142:290581
TITLE: The impact of P-glycoprotein on the disposition of drugs targeted for indications of the central nervous system: Evaluation using the MDR1A/1B knockout mouse model
AUTHOR(S): Doran, Angela; Obach, R. Scott; Smith, Bill J.; Hosea, Natilie A.; Becker, Stacey; Callegari, Ernesto; Chen, Cuiping; Chen, Xi; Choo, Edna; Cianfrogna, Julie; Cox, Loretta M.; Gibbs, John P.; Gibbs, Megan A.; Hatch, Heather; Hop, Cornelis E. C. A.; Kasman, Ilana N.; LaPerle, Jennifer; Liu, JianHua; Liu, Xingrong; Logman, Michael; Maclin, Debra; Nedza, Frank M.; Nelson, Frederick; Olson, Emily; Rahematpura, Sandhya; Raunig, David; Rogers, Sabrinia; Schmidt, Karl; Spracklin, Douglas K.; Szewc, Mark; Troutman, Matthew; Tseng, Elaine; Tu, Meihua; Van Deusen, Jeffrey W.; Venkatakrishnan, Karthik; Walens, Gary; Wang, Ellen Q.; Wong, Diane; Yasgar, Adam S.; Zhang, Chenghong
CORPORATE SOURCE: Departments of Pharmacokinetics, Dynamics, and Drug Metabolism, Pfizer Global Research and Development, Groton Laboratories, Groton, CT, USA
SOURCE: Drug Metabolism and Disposition (2005), 33(1), 165-174
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thirty-two structurally diverse drugs used for the treatment of various conditions of the central nervous system (CNS), along with two active metabolites, and eight non-CNS drugs were measured in brain, plasma, and cerebrospinal fluid in the P-glycoprotein (P-gp) knockout mouse model after s.c. administration, and the data were compared with corresponding data obtained in wild-type mice. Total brain-to-plasma (B/P) ratios for the CNS agents ranged from 0.060 to 24. Of the 34 CNS-active agents, only 7 demonstrated B/P area under the plasma concentration curve ratios between P-gp knockout and wild-type mice that did not differ significantly from unity. Most of the remaining drugs demonstrated 1.1- to 2.6-fold greater B/P ratios in P-gp knockout mice vs. wild-type mice. Three, risperidone, its active metabolite 9-hydroxyrisperidone, and metoclopramide, showed marked differences in B/P ratios between knockout and wild-type mice (6.6- to 17-fold). Differences in B/P ratios and cerebrospinal fluid/plasma ratios between wild-type and knockout animals were correlated. Through the use of this model, it appears that most CNS-active agents demonstrate at least some P-gp-mediated transport that can affect brain concns. However, the impact for the majority of agents is probably minor. The example of risperidone illustrates that even good P-gp substrates can still be clin. useful CNS-active agents. However, for such agents, unbound plasma concns. may need to be greater than values projected using receptor affinity data to achieve adequate receptor occupancy for effect.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 22 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:927018 HCAPLUS

DOCUMENT NUMBER: 141:388733
TITLE: Compositions of a cyclooxygenase-2 selective inhibitor and a sodium ion channel blocker for the treatment of central nervous system damage
INVENTOR(S): Stephenson, Diane T.; Taylor, Duncan P.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004093811	A2	20041104	WO 2004-US12383	20040421
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004224940	A1	20041111	US 2004-829009	20040421
PRIORITY APPLN. INFO.:			US 2003-464499P P	20030422
			US 2003-464830P P	20030423

OTHER SOURCE(S): MARPAT 141:388733
AB The invention provides compns. and methods for the treatment of central nervous system damage in a subject. More particularly, the invention provides a combination therapy for the treatment of a central nervous system ischemic condition or a central nervous system traumatic injury comprising the administration to a subject of a sodium ion channel blocker in combination with a cyclooxygenase-2 selective inhibitor. Use for the treatment of stroke is specifically claimed.

L16 ANSWER 23 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:802560 HCAPLUS
DOCUMENT NUMBER: 141:301459
TITLE: Novel formulations and method of treatment
INVENTOR(S): Buxton, Ian Richard; Currie, Robin; Dela-Cruz, Myrna A.; Goodson, Gary Wayne; Karolak, Wlodzimierz; Maleki, Mehran; Iyer, Vijay Mohan; Gopal, Muppirala; Parr, Alan Frank; Sidhu, Jagdev Singh; Stagner, Robert Allen; Vijay-Kumar, Akunuri Venkata
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 39 pp., Cont.-in-part of U.S. Ser. No. 629,177.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2004192690	A1	20040930	US 2003-726752		20031204
US 2005032799	A1	20050210	US 2003-629177		20030729
PRIORITY APPLN. INFO.:			GB 2002-17492	A	20020729
			GB 2002-17493	A	20020729
			GB 2003-13801	A	20030613
			US 2003-629177	A2	20030729

AB A sustained release formulation of lamotrigine or a pharmaceutically acceptable derivative thereof and methods of treatment and uses thereof are disclosed.

L16 ANSWER 24 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:740119 HCAPLUS
DOCUMENT NUMBER: 141:254567
TITLE: Methods and compositions for the treatment of chronic pain using dehydroepiandrosterone (DHEA) and derivatives thereof, alone or in combination with another drug
INVENTOR(S): Lucas, John M.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004075832	A2	20040910	WO 2004-US4861	20040219
WO 2004075832	A3	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006178354	A1	20060810	US 2005-546882	20050826
PRIORITY APPLN. INFO.:			US 2003-450217P	P 20030227
			WO 2004-US4861	W 20040219

AB The invention relates to the treatment of chronic pain using DHEA or derivs. thereof either alone or in combination with at least one other drug. The invention also includes compns. comprising DHEA or a derivative thereof and a second drug.

L16 ANSWER 25 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:120727 HCAPLUS
DOCUMENT NUMBER: 140:169680
TITLE: Sustained release formulations comprising lamotrigine
INVENTOR(S): Buxton, Ian Richard; Currie, Robin; Dela-Cruz, Myrna A.; Goodson, Gary Wayne; Karolak, Wlodzimierz; Maleki, Mehran; Iyer, Vijay Mohan; Muppirala, Gopal; Parr, Alan Frank; Sidhu, Jagdev Singh; Stagner, Robert Allen; Vijay-kumar, Akunuri Venkata
PATENT ASSIGNEE(S): Glaxo Group Limited, UK; et al.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004012741	A1	20040212	WO 2003-EP8368	20030728
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2493301	A1	20040212	CA 2003-2493301	20030728
AU 2003260336	A1	20040223	AU 2003-260336	20030728
EP 1524981	A1	20050427	EP 2003-766343	20030728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003013148	A	20050712	BR 2003-13148	20030728
CN 1681509	A	20051012	CN 2003-822371	20030728
JP 2005538113	T	20051215	JP 2004-525362	20030728
NO 2005000948	A	20050222	NO 2005-948	20050222
PRIORITY APPLN. INFO.:			GB 2002-17492	A 20020729
			GB 2002-17493	A 20020729
			GB 2003-13801	A 20030613
			WO 2003-EP8368	W 20030728

AB A sustained-release formulation, especially tablet, of lamotrigine or its derivative
for treatment of CNS disorder comprises (by weight) 2.5 to 80% lamotrigine or its derivative, 10 to 70% release retarding polymer, 0 to 70% diluent, 0 to 20% compression aid, and 0.1 to 2.5% lubricant. Substantially all the lamotrigine or a pharmaceutically acceptable derivative is released from the formulation in a period of 2 to 20 h after administration to a patient, producing an Area Under the Curve value of 80 to 125% and Cmax of about 30% less than that of an instant-release tablet containing the same amount of lamotrigine. For example, a tablet formulation (Diffcore device) was prepared comprising (i) a core containing lamotrigine 200 mg, a blend of hydroxypropyl Me celluloses K100LV 62.64 mg and E4M 45.36 mg, lactose monohydrate 90.4 mg, and magnesium stearate 1.6 mg, and (ii) an outer coat containing Eudragit L30 D-55 (30% weight/weight solution) 17.3 mg, Red
Iron Oxide 0.37 mg, tri-Et citrate 1.81 mg, glyceryl monostearate 0.494 mg, and Polysorbate 80 0.02 mg. The coating included orifices allowing the release of lamotrigine from the core.

L16 ANSWER 26 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:61937 HCAPLUS
DOCUMENT NUMBER: 141:342
TITLE: Brain access and anticonvulsant efficacy of carbamazepine, lamotrigine, and felbamate in ABCC2/MRP2-deficient TR- rats
AUTHOR(S): Potschka, Heidrun; Fedrowitz, Maren; Loescher, Wolfgang
CORPORATE SOURCE: Department of Pharmacology, Toxicology, and Pharmacy, School of Veterinary Medicine, Hannover, Germany

SOURCE: Epilepsia (2003), 44(12), 1479-1486
CODEN: EPILAK; ISSN: 0013-9580
PUBLISHER: Blackwell Publishing, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Different ATP (ATP)driven multidrug transporters have been described to be expressed in the luminal membrane of blood-brain barrier (BBB) endothelial cells. At this site, multidrug transporters have been suggested to restrict penetration of drugs into the brain. Increasing evidence suggests that overexpression of different multidrug transporters occurs in the region of the epileptic focus of pharmacoresistant epilepsy patients. Based on the assumption that antiepileptic drugs (AEDs) are substrates of these transporters, this overexpression may limit access of AEDs to epileptic neurons and may contribute to drug-refractoriness. In a recent study, overexpression of multidrug resistance protein 2 (ABCC2; MRP2) was reported in BBB endothelial cells of epileptic focal tissue from pharmacoresistant patients. With brain microdialysis, we recently demonstrated that the AED phenytoin is subject to transport by ABCC2 at the BBB, whereas phenobarbital does not seem to be a substrate of ABCC2. We investigated whether ABCC2 is functionally involved in transport of the AEDs carbamazepine (CBZ), lamotrigine (LTG), and felbamate (FBM) across the BBB. The distribution of these AEDs into the brain of ABCC2-deficient TR- rats was determined AED concns. in plasma and brain extracellular space of these mutant rats did not differ significantly from those of rats of the corresponding background strain. In the amygdalakindling model of epilepsy, the anticonvulsant efficacy of LTG and FBM was comparable in both groups of rats. In contrast, CBZ exhibited a higher anticonvulsant activity in kindled ABCC2-deficient rats as compared with nonmutant rats. In this present study, the microdialysis results gave no evidence that ABCC2 function modulates entry of CBZ, LTG, and FBM into the CNS of naive rats. However, ABCC2 deficiency was associated with an increased anticonvulsant response of CBZ in the kindling model. Future investigations are planned to identify the underlying mechanism for this difference, clarifying whether a pharmacokinetic difference is detectable only when brain access of CBZ is compared in kindled ABCC2-deficient rats and kindled nonmutant rats, which may have an increased expression of ABCC2 in response to seizures. The data substantiate that ABCC2-deficient TR- rats are a useful tool for defining the role of ABCC2 for transport of AEDs, and give evidence that the use of kindled TR- rats may provide important supplementary information.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 27 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:962301 HCAPLUS
DOCUMENT NUMBER: 141:1649
TITLE: Glutamate-dependent regulation of cholinergic phenotype in hypothalamic neurons
AUTHOR(S): Belousov, Andrei B.
CORPORATE SOURCE: Department of Cell and Molecular Biology, Tulane University, New Orleans, LA, 70118, USA
SOURCE: NeuroReport (2003), 14(18), 2445-2449
CODEN: NERPEZ; ISSN: 0959-4965
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Glutamate NMDA receptor antagonists are used clin. However, they have serious side effects, some of which are presumably due to an increase in acetylcholine transmission. The authors' previous expts. revealed

acetylcholine-dependent excitation in rat hypothalamic cultures after a chronic glutamate receptor blockade. Dextromethorphan, amantadine, and eliprodil are NMDA receptor antagonists. Lamotrigine inhibits synaptic glutamate release. These drugs are used clin. Here, using calcium imaging and immunocytochem., the authors demonstrate that a chronic treatment with each of these drugs induced acetylcholine activity and choline acetyltransferase immunoreactivity in rat hypothalamic (but not cortical) cultures. These data support the possibility that some side effects of anti-glutamate drugs in vivo may be due to the increase in cholinergic properties in certain regions of the CNS.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 28 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:769633 HCAPLUS
DOCUMENT NUMBER: 140:263619
TITLE: Relationship between lamotrigine oral dose, serum level and its inhibitory effect on CNS: insights from transcranial magnetic stimulation
AUTHOR(S): Tergau, Frithjof; Wischer, Stephan; Somal, Hardyal S.; Nitsche, Michael A.; Mercer, A. Joe; Paulus, Walter; Steinhoff, Bernhard J.
CORPORATE SOURCE: Department of Clinical Neurophysiology, University of Gottingen, Gottingen, D-37075, Germany
SOURCE: Epilepsy Research (2003), 56(1), 67-77
CODEN: EPIRES; ISSN: 0920-1211
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antiepileptic drug lamotrigine (LTG) is known to reduce cortical excitability evaluated by transcranial magnetic stimulation (TMS). We investigated the relationship between LTG oral dosages, serum levels and inhibitory effects on resting motor threshold (RMT), a parameter of motor system excitability assessed by TMS. In a randomized, placebo-controlled crossover study 16 male volunteers received 325 mg LTG as a single dose, as bi-hourly graded cumulative dose, or placebo. RMT and serum levels were measured before and after 2-8 h. With single dose, RMT elevation showed a poor but significant correlation to serum levels. With graded dose, serum levels as well as RMT increased dose-dependently with significant (P<0.0001) linear correlation. However, detailed comparison showed a high inter-individual variability in the relationship resembling a sigmoid correlation. Different mechanisms besides the sodium-channel blockage as the main mode of action of LTG are discussed to explain the diversity of individual dose-response relationships. Provided that the RMT elevation reflects the antiepileptic potential of LTG, TMS may be developed as a tool to monitor interindividual response of epilepsy patients to LTG treatment as well as to explore efficacy of other antiepileptic drugs with similar mode of action.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

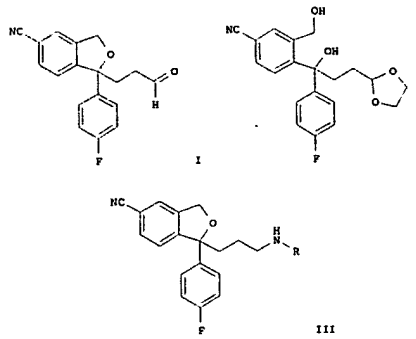
L16 ANSWER 29 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:376842 HCAPLUS
DOCUMENT NUMBER: 138:385297
TITLE: Methods for treating depression and other CNS disorders using enantiomerically enriched desmethyl- and didesmethyl- metabolites of citalopram
INVENTOR(S): Bush, Larry R.; Currie, Mark G.; Senanayake, Chris H.; Fang, Kevin Q.

PATENT ASSIGNEE(S): Sepracor, Inc., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040121	A1	20030515	WO 2002-US35408	20021105
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2465186	A1	20030515	CA 2002-2465186	20021105
AU 2002356903	A2	20030519	AU 2002-356903	20021105
EP 1446396	A1	20040818	EP 2002-802848	20021105
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002013949	A	20040831	BR 2002-13949	20021105
HU 200401934	A2	20050128	HU 2004-1934	20021105
JP 2005510518	T	20050421	JP 2003-542167	20021105
CN 1705654	A	20051207	CN 2002-822084	20021105
IN 2004KN00505	A	20060616	IN 2004-KN505	20040419
ZA 2004003409	A	20051026	ZA 2004-3409	20040505
US 2004266864	A1	20041230	US 2004-842055	20040507
NO 2004002013	A	20040514	NO 2004-2013	20040514

PRIORITY APPLN. INFO.: US 2001-337608P P 20011108
WO 2002-US35408 W 20021105

GI



I II III

AB This invention relates to the preparation of I and II and derivs. of I and II in their racemic, enantiomerically enriched, or optically pure forms. This invention further relates to novel compns. of matter containing enantiomerically enriched (-)-desmethylcitalopram (-)-III (R = Me), (+)-didesmethylcitalopram (+)-III (R = Me), or (-)-didesmethylcitalopram (-)-III (R = H) or mixts. thereof in optimal ratios. Contrary to prior teachings, the enantiomerically enriched citalopram metabolites disclosed herein possess potent serotonin reuptake inhibitory activity, with minimal inhibitory effects on the reuptake of other known monoamines, e.g., norepinephrine (NE) or dopamine (DA). For example, stepwise reaction of 1-oxo-1,3-dihydroisobenzofuran-5-carbonitrile with 4-fluorophenylmagnesium bromide and the chiral Grignard reagent, which was prepared from 2-(2-bromoethyl)-[1,3]dioxolane and Mg powder, in THF gave II. Cyclization using mesyl chloride in CH2Cl2, followed by reduction provided the I. Reaction of the aldehyde with (-)-tert-butylsulfinamide in the presence of Ti(OEt)4 in EtOH afforded the sulfinamide, which was reduced to the amine III (R = H) with 10% HCl in MeOH. Protection of the amine with BOC anhydride in the presence of TEA in CH2Cl2 provided the enantiomerically enriched isomers, which were separated on a chiral column and subsequently deprotected with TFA to give (+)-III (R = H) and (-)-III (R = H). In biol. assays, (-)-III (R = H) and (+)-III (R = H) strongly inhibited serotonergic 5-HT receptor activity with Ki values of 5.8 nM and 90 nM, resp., with little effect on NE and DA transporter activity. By comparison, racemic citalopram inhibited serotonin reuptake with a Ki of 3.9 nM. The present invention also discloses methods for treating disorders, dysfunctions and diseases for which inhibition of serotonin reuptake is therapeutically beneficial. In particular, the present invention discloses a method for treating various forms of depression and other CNS disorders with pharmaceutical compns. described herein.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 30 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:319348 HCAPLUS
DOCUMENT NUMBER: 138:331688
TITLE: Methods of suppressing microglial activation and systemic inflammatory responses
INVENTOR(S): Laskowitz, Daniel T.; Matthew, William D.; McMillian, Michael
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 48 pp., Cont.-in-part of U.S. Ser. No. 957,909.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003077641	A1	20030424	US 2002-252120	20020923
US 2002164789	A1	20021107	US 2001-957909	20010921
PRIORITY APPLN. INFO.:			US 1998-77551P P	19980311
			US 1999-260430 B2	19990301
			US 2001-957909 A2	20010921

AB Methods of suppressing the activation of microglial cells in the Central Nervous System (CNS), methods of ameliorating or treating the neurol. effects of cerebral ischemia or cerebral inflammation, and methods of combating specific diseases that affect the CNS by administering a compound that binds to microglial receptors and prevents or reduces microglial activation are described. ApoE receptor binding peptides that may be used in the methods of the invention are also described, as are methods of using such peptides to treat peripheral inflammatory conditions such as sepsis. Also described are methods of screening compds. for the ability to suppress or reduce microglial activation. Injection of ApoE (133-149) in mice suppressed serum levels of TNFα and IL-6 following LPS administration.

L16 ANSWER 31 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:854041 HCAPLUS
DOCUMENT NUMBER: 139:111447
TITLE: Therapeutic Drug Monitoring of Lamotrigine in Patients Suffering from Resistant Partial Seizures
AUTHOR(S): Benetello, Pierpaola; Furlanut, Marco; Baraldo, Massimo; Tonon, Agnese; Furlanut, Mario
CORPORATE SOURCE: Department of Neurological Sciences, University of Padua, Padua, Italy
SOURCE: European Neurology (2002), 48(4), 200-203
CODEN: EUNEAP; ISSN: 0014-3022
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sixty patients, all potential candidates for ongoing lamotrigine (LTG) treatment as add-on therapy for resistant partial seizures and receiving carbamazepine (CBZ) and/or valproate (VPA) treatment, were submitted to therapeutic drug monitoring (TDM). The aim was to evaluate the possible relation between serum levels and the clin. effect of LTG, to verify whether CNS toxicity has to be considered the result of a pharmacokinetic or a pharmacodynamic interaction with CBZ, and to

investigate whether possible changes in the clin. response during long-term treatment are dependent on LTG serum level variations. Sixteen patients achieved complete control, 25 a ≥50% reduction in seizures, the remainder did not respond. Mean LTG serum concns. were higher in responders than in nonresponders, the difference being statistically insignificant. The best results were observed in VPA-cotreated patients with the highest LTG blood levels. CNS toxicity occurred after giving LTG to subjects who subsequently developed the highest LTG concns., whereas CNS toxicity seemed unrelated to CBZ and CBZ-epoxide serum concns. No decrease in LTG, CBZ and VPA serum levels was observed even in patients showing a reduction in the response during long-term treatment.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 32 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:797249 HCAPLUS
DOCUMENT NUMBER: 139:29927
TITLE: Anticonvulsants in central pain
AUTHOR(S): Finnerup, Nanna B.; Gottrup, Hanne; Jensen, Troels S.
CORPORATE SOURCE: Department of Neurology and Danish Pain Research Centre, Aarhus University Hospital, Aarhus, 8000, Den.
SOURCE: Expert Opinion on Pharmacotherapy (2002), 3(10), 1411-1420
CODEN: EOPHP7; ISSN: 1465-6566
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Treatment of central neuropathic pain (CP) following lesions of the CNS is a great challenge to the clinician. Preclin. and clin. studies indicate that neuronal hyperexcitability in damaged areas of the central nervous system plays a major role in the development of CP. Anticonvulsants are thought to act by increasing γ-aminobutyric acid-mediated inhibition, decreasing abnormal neuronal hyperexcitability by modulating sodium and calcium channels or by inhibiting excitatory amino acid actions. The resulting inhibition of excess neuronal activity is thought to be the basis for the use of anticonvulsants in epilepsy as well as neuropathic pain. Both first-generation anticonvulsant drugs (e.g., phenytoin, benzodiazepines, valproate and carbamazepine) and second-generation anticonvulsant drugs (e.g., lamotrigine, gabapentin and topiramate) are used in CP conditions. However, few randomized controlled trials on the treatment of this condition have been published. Present suggestions for anticonvulsant treatment of CP are lamotrigine as the first choice, followed by gabapentin or carbamazepine/oxcarbazepine. These compds. are considered as effective as the antidepressant amitriptyline.
REFERENCE COUNT: 106 THERE ARE 106 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 33 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:672895 HCAPLUS
DOCUMENT NUMBER: 138:297430
TITLE: Lamotrigine derivatives and riluzole inhibit INa,P in cortical neurons
AUTHOR(S): Spadoni, Francesca; Hainsworth, Atticus Henry; Mercuri, Nicola Biagio; Caputi, Luigi; Martella, Giuseppina; Lavaroni, Franco; Bernardi, Giorgio; Stefani, Alessandro
CORPORATE SOURCE: IRCCS Fondazione Santa Lucia, Rome, Italy

SOURCE: NeuroReport (2002), 13(9), 1167-1170
CODEN: NERPEZ; ISSN: 0959-4965
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The persistent, slowly inactivating fraction of the sodium current (INa,P) is involved in key functions in the CNS such as dendritic integration of synaptic inputs and cellular excitability. We have studied whether established anti-epileptic drugs and neuroprotective agents target the persistent sodium current. Two lamotrigine derivs. (eipatrigine and 202W92) and riluzole inhibited the persistent sodium current at low, therapeutic concns. In contrast, lamotrigine and the classical antiepileptic agents phenytoin and valproic acid blocked the fast-inactivating sodium channel but failed to affect the persistent fraction. The ability to influence either mode of channel activity may represent a defining feature of each drug subclass, changing profoundly their clin. indications. Given the damaging role of a sustained influx of sodium in both pharmaco-resistant seizures or excitotoxic insults, we suggest the utilization of drugs that suppress the persistent conductance.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 34 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:488246 HCAPLUS
DOCUMENT NUMBER: 137:57576
TITLE: Methods and compositions using ion-dependent cotransporter modulators for treating conditions of the central and peripheral nervous systems using non-synaptic mechanisms
INVENTOR(S): Hochman, Daryl W.
PATENT ASSIGNEE(S): Cytoscan Sciences L.L.C., USA
SOURCE: U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S. Ser. No. 470,637.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002082252	A1	20020627	US 2002-56528		20020123
US 6495601	B1	20021217	US 1999-470637		19991222
US 2005267103	A1	20051201	US 2005-101000		20050407
US 2006025387	A1	20060202	US 2005-130945		20050517
US 2006089350	A1	20060427	US 2005-251724		20051017
US 2006035914	A1	20060216	US 2005-259532		20051025
PRIORITY APPLN. INFO.:			US 1998-113620P	P	19981223
			US 1999-470637	A2	19991222
			US 2001-263830P	P	20010123
			US 2002-56528	A2	20020123
			US 2005-101000	A2	20050407
			US 2005-130945	A2	20050517

AB The invention discloses methods and compns. for treating selected conditions of the central and peripheral nervous systems employing non-synaptic mechanisms. More specifically, one aspect of the invention provides methods and materials for treating seizure and seizure disorders, epilepsy, status epilepticus, migraine, spreading depression, intracranial hypertension; for treating the pathophysiol. effects of head trauma,

stroke, ischemia and hypoxia; for treating or protecting from the pathophysiol. effects of neurotoxic agents such as ethanol; and for treating neurophsyciatric disorders and central nervous system edema by administering agents that modulate ionic concns. and/or ionic gradients in the brain, particularly ion-dependent or cation-chloride cotransporter antagonists. Electrolyte cotransport antagonists and combinations of such compns. with other agents for treating various conditions are disclosed. The invention also discloses methods and compns. for treating pain by administering ion-dependent cotransporter antagonists. Methods and compns. for enhancing cortical function, e.g. in centers of cognition, learning, and memory, by administering ion-dependent cotransporter agonists are disclosed.

L16 ANSWER 35 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:375796 HCAPLUS
DOCUMENT NUMBER: 137:5563
TITLE: Diet enriched with omega-3 fatty acids alleviates convulsion symptoms in epilepsy patients
AUTHOR(S): Schlanger, Simon; Shinitzky, Meir; Yam, Daniel
CORPORATE SOURCE: The Kalanit Institute for the Retarded Child, Rishon LeZion, Israel
SOURCE: Epilepsia (2002), 43(1), 103-104
CODEN: EPILAK; ISSN: 0013-9580
PUBLISHER: Blackwell Publishing, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We examined whether a dietary supplement containing omega-3 polyunsatd. fatty acids (n-3 PUFAs) can alleviate and/or reduce the frequency of epileptic seizures in patients with central nervous system (CNS) diseases treated with anticonvulsive drugs (ACDs). A special spread containing 65% n-3 PUFAs was added to the daily diet. The patients consumed 5 g of this spread at every breakfast for 6 mo. Five patients completed the study. In all of them, a marked reduction in both frequency and strength of the epileptic seizures was recorded. Incorporation of the dietary supplement containing n-3 PUFAs may be beneficial in suppression of some cases of epileptic seizures.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 36 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:195041 HCAPLUS
DOCUMENT NUMBER: 137:91443
TITLE: GABA and glutamate in migraine
AUTHOR(S): D'Andrea, Giovanni; Granella, Franco; Cataldini, Morena; Verdelli, Flavio; Balbi, Tiziana
CORPORATE SOURCE: Headache and Related Disorders Center, Pathology Unit, Este-Monselice Hospital, Este-Monselice, Italy
SOURCE: Journal of Headache and Pain (2001), 2(Suppl. 1), S57-S60
CODEN: JHPOAT; ISSN: 1129-2369
PUBLISHER: Springer-Verlag Italia Srl
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. GABA and glutamic acid are the main inhibitory and excitatory neurotransmitters of central nervous system. Among other functions they modulate the pain threshold in the CNS. For this reason it has been hypothesized that anomalies of GABA and glutamate turn-over may play a role in migraine pathogenesis. In this review are discussed the evidences in favor of this hypothesis. A derangement of GABA may be an

important factor in the occurrence of migraine attacks and their recurrence, whereas high level of glutamic acid may represent a biochem. marker of the neuronal hyperexcitability that may be the underlying cause of the aura. The pharmacol. modulation of metabolism of both neurotransmitters is a promising approach to improve migraine therapy. In particular the studies presented here suggest that gabaergic drugs may be useful in migraine without aura, antiglutamatergic drugs are indicated to treat migraine with aura.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 37 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:10280 HCAPLUS
DOCUMENT NUMBER: 136:64150
TITLE: GABA-ergic agonists for the treatment of age-related brain cortical dysfunction
INVENTOR(S): Leventhal, Audie G.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002000221	A1	20020103	WO 2001-US19719		20010620
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2413405	A1	20020103	CA 2001-2413405		20010620
AU 2001068609	A5	20020108	AU 2001-68609		20010620
EP 1303280	A1	20030423	EP 2001-946582		20010620
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
US 2004023952	A1	20040205	US 2002-311821		20021217
AU 2006203432	A1	20060831	AU 2006-203432		20060809
PRIORITY APPLN. INFO.:			US 2000-213388P	P	20000623
			US 2001-277427P	P	20010320
			WO 2001-US19719	W	20010620

AB Methods are disclosed for the improvement of age-related decreases in cortical function by increasing the activity of inhibitory pathways, such as GABA-ergic pathways, in the central nervous system. In particular examples, subjects with age-related decreases in cortical function are treated by administration of therapeutically effective amts. of a GABA-ergic agonist. The disclosed methods also enable screening for drugs that inhibit an age-related decline in cortical function, for example by exposing a subject to a test agent, and measuring an increase in GABA-ergic cortical inhibitory activity.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 38 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:904923 HCAPLUS
DOCUMENT NUMBER: 136:181219
TITLE: Effect of lamotrigine on the Ca2+-sensing cation current in cultured hippocampal neurons
AUTHOR(S): Xiong, Zhi-Gang; Chu, Xiang-Ping; MacDonald, J. F.
CORPORATE SOURCE: Robert S. Dow Neurobiology Laboratories, Legacy Clinical Research and Technology Center, Portland, OR, 97232, USA
SOURCE: Journal of Neurophysiology (2001), 86(5), 2520-2526
CODEN: JONEA4; ISSN: 0022-3077
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

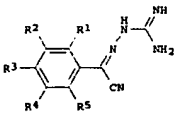
AB Concns. of extracellular calcium ([Ca2+]e) in the CNS decrease substantially during seizure activity. The authors have demonstrated previously that decreases in [Ca2+]e activate a novel calcium-sensing nonselective cation (csNSC) channel in hippocampal neurons. Activation of csNSC channels is responsible for a sustained membrane depolarization and increased neuronal excitability. This study has suggested that the csNSC channel is likely involved in generating and maintaining seizure activities. In the present study, the effects of anti-epileptic agent lamotrigine (LTG) on csNSC channels were studied in cultured mouse hippocampal neurons using patch-clamp techniques. At a holding potential of -60 mV, a slow inward current through csNSC channels was activated by a step reduction of [Ca2+]e from 1.5 to 0.2 mM. LTG decreased the amplitude of csNSC currents dose dependently with an IC50 of 171 ± 25.8 (SE) μM. The effect of LTG was independent of membrane potential. In the presence of 300 μM LTG, the amplitude of csNSC current was decreased by 31 ± 3% at -60 mV and 29 ± 2.9% at +40 mV ($P > 0.05$). LTG depressed csNSC current without affecting the potency of Ca2+ block of the current (IC50 for Ca2+ block of csNSC currents in the absence of LTG: 145 ± 18 μM; in the presence of 300 μM LTG: 136 ± 10 μM, $n = 5$, $P > 0.05$). In current-clamp recordings, activation of csNSC channel by reducing the [Ca2+]e caused a sustained membrane depolarization and an increase in the frequency of spontaneous firing of action potentials. LTG (300 μM) significantly inhibited csNSC channel-mediated membrane depolarization and the excitation of neurons. Fura-2 ratiometric Ca2+ imaging experiment showed that LTG also inhibited the increase in intracellular Ca2+ concentration induced by csNSC channel activation. The effect of LTG on csNSC channels may partially contribute to its broad spectrum of anti-epileptic actions.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 39 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:631908 HCAPLUS
DOCUMENT NUMBER: 135:195578
TITLE: Process for preparing substituted benzoyl cyanide amidinohydrazones as intermediates for synthesis of 3,5-diamino-6-phenyl-1,2,4-triazines
INVENTOR(S): Nadaka, Vladimir; Lexner, Jael; Kaspi, Joseph
PATENT ASSIGNEE(S): Chemagis Ltd., Israel
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1127873	A2	20010829	EP 2001-103660	20010223
EP 1127873	A3	20030507		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
IL 134730	A	20031031	IL 2000-134730	20000225
CA 2337280	A1	20010825	CA 2001-2337280	20010215
HU 200100740	A2	20011128	HU 2001-740	20010215
US 2001025118	A1	20010927	US 2001-789634	20010222
US 6329521	B2	20011211		

PRIORITY APPLN. INFO.: IL 2000-134730 A 20000225
OTHER SOURCE(S): CASREACT 135:195578; MARPAT 135:195578
GI



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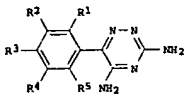

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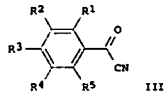


III

AB The title compds. [I; R1-R5 = H, halo, alkyl, etc.], useful as intermediates for synthesis of 1,2,4-triazines II (active in the treatment of CNS disorders), were prepared by reacting the benzoyl cyanides III with aminoguanidine bicarbonate in a mixture of a water-soluble solvent and polyphosphoric acid. Thus, reacting 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in the presence of polyphosphoric acid in MeCN afforded 2,3-dichlorobenzoyl cyanide amidinohydrazone which was then heated under reflux in PrOH to give 2,3-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine.

L16 ANSWER 40 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:237425 HCAPLUS
DOCUMENT NUMBER: 130:291518
TITLE: Analysis of CSF amino acids in young patients with generalized refractory epilepsy during an add-on study with lamotrigine
AUTHOR(S): Eriksson, Ann-Sofie; O'Connor, William T.
CORPORATE SOURCE: Department of Pediatrics, Karolinska Hospital,

Stockholm, Swed.
SOURCE: Epilepsy Research (1999), 34(1), 75-83
CODEN: EPIRES; ISSN: 0920-1211
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of add-on administration of lamotrigine (1-12 mg/kg per day, 2-12 mo) on the levels of neurotransmission related amino acids including γ-aminobutyric acid (GABA), glutamate, aspartate, glycine and antiepileptic drugs (AEDs) in lumbar cerebrospinal fluid (CSF) was studied in 22 children and young adults with generalized therapy resistant epilepsy. Two lumbar punctures were performed, one prior to, and one following a mean of 5 mo (2-12 mo) of lamotrigine treatment. Lamotrigine decreased seizure incidence and severity in 12 of the 22 patients without influencing CSF GABA, glutamate, aspartate or glycine levels. Lamotrigine did not alter the concns. of AEDs in CSF or plasma. However, CSF GABA levels were 86% higher in those patients also treated with γ-vinyl-GABA (vigabatrin, GVG) compared with patients treated with other combinations and this was not altered by co-medication with lamotrigine. The proposed mechanism of action of lamotrigine, namely that it may inhibit glutamate release in the CNS, is not reflected by changes in CSF glutamate levels. The present findings indicate that CSF GABA, glutamate, aspartate and glycine levels may not be useful as in vivo neurochem. markers in young patients responding to the therapeutic dose of lamotrigine used in this study.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 41 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:567031 HCAPLUS
DOCUMENT NUMBER: 129:270545
TITLE: Mechanisms of deafferentation-induced plasticity in human motor cortex
AUTHOR(S): Ziemann, Ulf; Hallett, Mark; Cohen, Leonardo G.
CORPORATE SOURCE: Human Cortical Physiology Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, 20892-1428, USA
SOURCE: Journal of Neuroscience (1998), 18(17), 7000-7007
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Deafferentation induces rapid plastic changes in the cerebral cortex, probably via unmasking of pre-existent connections. Several mechanisms may contribute, such as changes in neuronal membrane excitability, removal of local inhibition, or various forms of short- or long-term synaptic plasticity. To understand further the mechanisms involved in cortical plasticity, we tested the effects of CNS-active drugs in a plasticity model, in which forearm ischemic nerve block (INB) was combined with low-frequency repetitive transcranial magnetic stimulation (rTMS) of the deafferented human motor cortex. RTMS was used to upregulate the plastic changes caused by INB. We studied six healthy subjects. In two control sessions without drug application, INB plus rTMS increased the motor-evoked potential (MEP) size and decreased intracortical inhibition (ICI) measured with single- and paired-pulse TMS in the biceps brachii muscle proximal to INB. A single oral dose of the benzodiazepine lorazepam (2 mg) or the voltage-gated Na+ and Ca2+ channel blocker lamotrigine (300 mg) abolished these changes. The NMDA receptor blocker dextromethorphan (150 mg) suppressed the reduction in ICI but not the increase

in MEP size. With sleep deprivation, used to eliminate sedation as a major factor of these drug effects, INB plus rTMS induced changes similar to that seen in the control sessions. The findings suggest that (1) the INB plus rTMS-induced increase in MEP size involves rapid removal of GABA-related cortical inhibition and short-term changes in synaptic efficacy dependent on Na+ or Ca2+ channels and that (2) the long-lasting (>60 min) reduction in ICI is related to long-term potentiation-like mechanisms given its duration and the involvement of NMDA receptor activation.
REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 42 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:105002 HCAPLUS
DOCUMENT NUMBER: 128:213312
TITLE: Carbamazepine toxicity with lamotrigine: pharmacokinetic or pharmacodynamic interaction?
AUTHOR(S): Besag, F. M. C.; Berry, D. J.; Pool, F.; Newbery, J. E.; Subel, B.
CORPORATE SOURCE: St Piers Lingfield, Surrey, RH7 6PW, UK
SOURCE: Epilepsia (1998), 39(2), 183-187
CODEN: EPILAK; ISSN: 0013-9580
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In order to determine whether the toxicity that occurs in some patients when lamotrigine (LTG) is added to carbamazepine (CBZ) is the result of either a pharmacokinetic or a pharmacodynamic interaction, escalating LTG doses were added to ongoing CBZ treatment in 47 patients. All patients had blood samples collected for drug concentration measurement, including the epoxide metabolite of CBZ, before starting LTG treatment and after stabilizing at each dose escalation. Patients also were examined for signs of toxicity. After LTG was introduced, nine patients demonstrated clin. signs of CNS toxicity, mainly diplopia and dizziness. There was no significant ($p = 0.05$) change in the serum concns. of either CBZ or its epoxide metabolite when LTG was added either to the group as a whole or to the nine patients who experienced adverse CNS effects. LTG serum concns. also were below the level at which the common signs of LTG toxicity, such as nausea, vomiting, or unsteadiness, are more likely to occur. In seven of the nine patients who exhibited CNS toxicity, CBZ serum concns. were >8 mg/L on LTG introduction. Toxicity is more likely to occur when LTG is added to CBZ if the initial CBZ level is high, typically >8 mg/L. This appears to be the result of a pharmacodynamic interaction. A reduction of CBZ dose usually resolves the toxicity, allowing the LTG dose to be escalated to maximal effect. It is not usually necessary to stop either drug.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 43 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:638497 HCAPLUS
DOCUMENT NUMBER: 125:315860
TITLE: Lamotrigine monotherapy: An overview
AUTHOR(S): Brodie, M. J.
CORPORATE SOURCE: WESTERN INFIRMARY, UNIVERSITY DEPARTMENT MEDICINE AND THERAPEUTICS, Glasgow, UK
SOURCE: International Congress and Symposium Series - Royal Society of Medicine (1996), 214(Lamotrigine--A

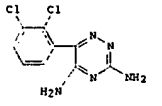
Brighter Future), 43-49
CODEN: RMISDU; ISSN: 0142-2367
PUBLISHER: Royal Society of Medicine Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with .apprx.5 refs. In a pooled population of 784 patients with newly-diagnosed epilepsy participating in comparative monotherapy trials, 443 were randomized to lamotrigine, 246 to carbamazepine and 95 to phenytoin. Overall, fewer patients were withdrawn due to adverse events on lamotrigine than with the older drugs (lamotrigine 9.5%, carbamazepine 19.1%, phenytoin 18.9%). Central nervous system (CNS) problems resulting in withdrawal, in particular, were infrequent with lamotrigine (lamotrigine 2.5%, carbamazepine 7.7%, phenytoin 7.4%). Withdrawal due to rash occurred in 6.1% of patients on lamotrigine, 8.9% on carbamazepine and 5.3% on phenytoin. The rash rate leading to withdrawal with lamotrigine appeared to relate to the initiation dose (100 mg, 11.8%; 50 mg, 9.2%; 25 mg, 2.2%). It is sometimes appropriate to substitute lamotrigine monotherapy for other antiepileptic drug treatments. Schedules for substituting lamotrigine in patients established on phenytoin, carbamazepine or sodium valproate are outlined. In the comparative monotherapy trials, the most popular lamotrigine doses were 150-200 mg daily. In studies in which concomitant antiepileptic drugs (AEDs) were withdrawn to achieve lamotrigine monotherapy, some patients took as much as 700 mg lamotrigine daily. Clin. experience to date does not suggest the existence of a relationship between the plasma lamotrigine concentration and its efficacy or toxicity. Data and case reports from a prospective study in Glasgow relating lamotrigine dosage and concentration to seizure control and the emergence of side effects are presented.

L16 ANSWER 44 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:94551 HCAPLUS
DOCUMENT NUMBER: 124:194132
TITLE: The effects of anticonvulsants on 4-aminopyridine-induced bursting: in vitro studies on rat peripheral nerve and dorsal roots
AUTHOR(S): Lees, G.
CORPORATE SOURCE: Dep. Academic Anaesthetics, Imperial College Medicine, London, W2 1NY, UK
SOURCE: British Journal of Pharmacology (1996), 117(3), 573-9
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Aminopyridines have been used as beneficial symptomatic treatments in a variety of neurol. conditions including multiple sclerosis but have been associated with considerable toxicity in the form of abdominal pain, paraesthesias and (rarely) convulsions. Extracellular and intracellular recording was used to characterize action potentials in rat sciatic nerves and dorsal roots and the effects of 4-aminopyridine (4-AP). In sciatic nerve trunks, 1 mM 4-AP produced pronounced after potentials at room temperature secondary to regenerative firing in affected axons (5-10 spikes per stimulus). At physiol. temps., after potentials (2-3 spikes) were greatly attenuated in peripheral axons. 4-AP evoked more pronounced and prolonged after discharges in isolated dorsal roots at 37°C (3-5.5 mV and 80-100 ms succeeded by a smaller inhibitory/depolarizing voltage shift) which were used to assess the effects of anticonvulsants. Phenytoin, carbamazepine and lamotrigine dose-dependently reduced the area of 4-AP-induced after potentials at 100 and 320 μM but the amplitude of

compound action potentials (evoked at 0.5 Hz) was depressed in parallel. The tonic block of sensory action potentials by all three drugs (at 320 μM) was enhanced by high frequency stimulation (5-500 Hz). The lack of selectivity of these frequency-dependent Na+ channel blockers for burst firing, compared to low-frequency spikes, is discussed in contrast to their effects on 4-AP-induced seizures and paroxysmal activity in CNS tissue (which is associated with large and sustained depolarizing plateau potentials). In conclusion, these in vitro results confirm the marked sensitivity of sensory axons to 4-AP (the presumptive basis for paraesthesias). Burst firing was not preferentially impaired at relatively high concns. suggesting that anticonvulsants will not overcome the toxic peripheral actions of 4-AP in neurol. patients.

L16 ANSWER 45 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:531450 HCAPLUS
DOCUMENT NUMBER: 119:131450
TITLE: Studies on the mechanism of action of the novel anticonvulsant lamotrigine (Lamictal) using primary neuroglial cultures from rat cortex
AUTHOR(S): Lees, George; Leach, Michael J.
CORPORATE SOURCE: Dep. Pharmacol., Wellcome Res. Lab., Beckenham/Kent, BR3 3BS, UK
SOURCE: Brain Research (1993), 612(1-2), 190-9
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Whole cell and perforated patch clamp expts. were conducted on cultured cortical rat neurons (7-21 days in vitro) in order to determine the effects of the anticonvulsant and glutamate release inhibitor lamotrigine (10-100 μM), on CNS receptors and ion channels. The compound inhibited, indiscriminately, both excitatory and inhibitory synaptic events which occurred spontaneously in cultured neural circuits. The drug did not mimic diazepam as a pos. modulator of GABAA currents. In the presence of tetrodotoxin, voltage-gated potassium currents and composite currents evoked by L-glutamate were not significantly modulated even at the highest dose. Unitary, fast, presumptive-sodium spikes, evoked at low frequencies, were not blocked significantly by lamotrigine. In contrast, burst firing induced by pulsed application of L-glutamate or potassium ions was markedly depressed at 10 μM. Presumptive calcium currents were inhibited by lamotrigine at 100 μM. It is proposed that the drug inhibits epileptiform burst firing preferentially by state/activity dependent interactions with voltage and gated cation channels. Potential mechanisms for inhibition of glutamate release are discussed.

L16 ANSWER 46 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:102360 HCAPLUS
DOCUMENT NUMBER: 104:102360
TITLE: Lamotrigine (BW430C), a potential anticonvulsant. Effects on the central nervous system in comparison with phenytoin and diazepam
AUTHOR(S): Cohen, A. F.; Ashby, L.; Crowley, D.; Land, G.; Peck, A. W.; Miller, A. A.
CORPORATE SOURCE: Wellcome Res. Lab., Beckenham/Kent, UK
SOURCE: British Journal of Clinical Pharmacology (1985), 20(6), 619-29
CODEN: BCPHBM; ISSN: 0306-5251
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Healthy male volunteers received phenytoin [57-41-0] 0.5 and 1 g, lamotrigine (I) [84057-84-1] (a new anticonvulsant) 120 and 240 mg, diazepam [439-14-5] 10 mg and placebo orally in a double-blind, cross-over, randomized trail. Maximum drug concns. at 4 h, measured in plasma were 11.5 μg/mL for phenytoin and 2.7 μg/mL for lamotrigine. These levels were in the therapeutic range for phenytoin and the putative therapeutic range for lamotrigine. Side effects after diazepam (mainly sedation) and phenytoin (mainly unsteadiness) differed markedly from lamotrigine which produced no important side effects. Subjective effects as measured by visual analog scales were caused by phenytoin and diazepam but not by lamotrigine. Diazepam impaired eye movements, adaptive tracking and body sway. Phenytoin impaired adaptive tracking, increased body sway and impaired smooth pursuit eye movement. Lamotrigine produced only a possible slight increase in body sway. There were significant correlations between performance and saliva levels of phenytoin and diazepam. The tests used were suitable for monitoring central nervous system (CNS) effects of anticonvulsants and lamotrigine possibly could have a more favorable CNS side effect than phenytoin.

=> d his

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FILE 'REGISTRY' ENTERED AT 16:55:37 ON 04 APR 2007
L1 STRUCTURE UPLOADED
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L3 128 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 16:56:47 ON 04 APR 2007
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E US20050238724/PN,PRN,AN
L5 0 S E3/RN
L6 1 S E3

FILE 'REGISTRY' ENTERED AT 16:58:38 ON 04 APR 2007
L7 0 S L6

FILE 'HCAPLUS' ENTERED AT 17:00:04 ON 04 APR 2007
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S LAMOTRIGINE/CN

FILE 'REGISTRY' ENTERED AT 17:00:26 ON 04 APR 2007
L8 1 S LAMOTRIGINE/CN

FILE 'HCAPLUS' ENTERED AT 17:00:27 ON 04 APR 2007
L9 1265 S L8

L10 27 S "3,5-DIAMINO-6-(2,3-DICHLOROPHENYL)-1,2,4-TRIAZINE"

FILE 'REGISTRY' ENTERED AT 17:02:26 ON 04 APR 2007
L11 1 S 84057-84-1/RN

FILE 'HCAPLUS' ENTERED AT 17:02:48 ON 04 APR 2007
L12 1265 S L11
L13 111187 S L10 OR L12 AND PARTICLE OR GRANULE
L14 0 S L12 (N) PARTICLE
L15 0 S L12 (W) PARTICLE
L16 46 S L12 AND CNS

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=> s aronhime,j?/au or samburski,g?/au
           86 ARONHIME,J?/AU
            8 SAMBURSKI,G?/AU
L17        91 ARONHIME,J?/AU OR SAMBURSKI,G?/AU

=> s aronhime,j?/au and samburski,g?/au
           86 ARONHIME,J?/AU
            8 SAMBURSKI,G?/AU
L18         3 ARONHIME,J?/AU AND SAMBURSKI,G?/AU

=> d l18 1-3 ibib abs

L18  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        2007:259910  HCAPLUS
DOCUMENT NUMBER:         146:281059
TITLE:                   Solid particulate tadalafil having a bimodal particle
                         size distribution
INVENTOR(S):             Aronhime, Judith; Samburski, Guy;
                         Ovadya, Yhoshoa
PATENT ASSIGNEE(S):      Teva Pharmaceutical Industries Ltd., Israel; Teva
                         Pharmaceuticals USA, Inc.
SOURCE:                  PCT Int. Appl., 19pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

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     WO 2007027612         A2    20070308    WO 2006-US33541         20060829
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             GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
             KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
             MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
             RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                       US 2005-712589P     P  20050829
AB   Provided is a solid particulate tadalafil having a bimodal particle size
     distribution.  The solid particulate tadalafil is useful for the manufacture of
     a medicament for the treatment of sexual dysfunction.  Thus, 2 g of a
     solid particulate tadalafil having a bimodal particle size distribution
     were prepared by combining 0.38 g of large particle size tadalafil and 1.62
     g of small particle size tadalafil.  Calcn. of the amount of large particle
     size particulate tadalafil was presented.

L18  ANSWER 2 OF 3  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        2006:543943  HCAPLUS
DOCUMENT NUMBER:         145:45919
TITLE:                   Process for the preparation of ezetimibe polymorphic
                         crystalline forms
INVENTOR(S):             Aronhime, Judith; Koltai, Tamas;
                         Samburski, Guy; Lehrman, Ori; Izsak, Reuven
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PATENT ASSIGNEE(S):      Teva Pharmaceutical Industries Ltd., Israel; Teva
                         Pharmaceuticals Usa, Inc.
SOURCE:                  PCT Int. Appl., 54 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

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     WO 2006060808         A1    20060608    WO 2005-US44065         20051205
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             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
             MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
             SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
             VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
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             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
     US 2006160785         A1    20060720    US 2005-295141          20051205
PRIORITY APPLN. INFO.:                       US 2004-632543P     P  20041203
                                             US 2005-649139P     P  20050203
                                             US 2005-668571P     P  20050406
                                             US 2005-687316P     P  20050606
                                             US 2005-712781P     P  20050830
                                             US 2005-717275P     P  20050914
AB   Processes are described for preparing polymorphic crystalline forms of
ezetimibe,
     such as ezetimibe Form A or Form B, for example, by precipitating ezetimibe
from
     selected solvents.  Some forms may be transformed into different forms at
     elevated temps., or under various humidity conditions, or by
     micronization.
REFERENCE COUNT:         8     THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18  ANSWER 3 OF 3  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        2003:875073  HCAPLUS
DOCUMENT NUMBER:         139:354488
TITLE:                   Pharmaceutical composition containing lamotrigine
                         particles of defined morphology
INVENTOR(S):             Aronhime, Judith; Samburski, Guy
PATENT ASSIGNEE(S):      Teva Pharmaceutical Industries Ltd., Israel; Teva
                         Pharmaceuticals USA, Inc.
SOURCE:                  PCT Int. Appl., 24 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2003090693         A2    20031106    WO 2003-US13002         20030423
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EAST Search History

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S1	0	lamotrigene same particle adj size	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/24 07:32
S2	7	lamotrigene	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/04/04 15:24
S3	23310	particles same specific adj surface adj area	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/23 17:04
S4	163	S3 and pharmaceutical adj composition	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/23 17:51
S5	0	lamotrigene same Teva adj Pharmaceutical?	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/23 17:54
S6	0	lamotrigene same Teva	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/23 17:52
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S8	1	("5861179").PN.	US-PGPUB; USPAT	OR	OFF	2006/08/23 18:21
S9	0	bet near particle adj size near surface adj area	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/24 07:33
S10	1134	particle adj size near surface adj area	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2006/08/24 07:43
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S13	1	("4602017").PN.	US-PGPUB; USPAT	OR	OFF	2006/08/24 15:06

EAST Search History

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S20	5	((GUY) near2 (SAMBURSKI)).INV.	US-PGPUB; USPAT; USOCR	OR	ON	2007/04/04 15:20
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EAST Search History

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S39	38	S36 and particl??	US-PGPUB; USPAT; USOCR	OR	ON	2007/04/04 16:15

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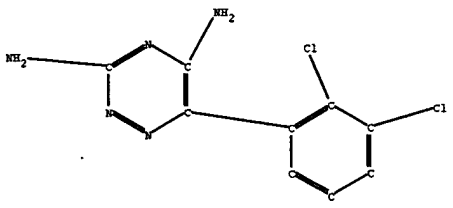
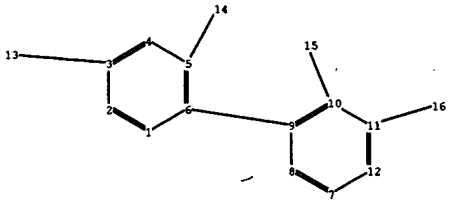
STN
lwl
4/4/07





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ring nodes :
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chain bonds :
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ring bonds :
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exact/norm bonds :
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exact bonds :
6-9 10-15 11-16
normalized bonds :
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Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS

10/511987 LAMOTRIGINE reg no-text search USPGPUB search

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L3            128 S L1 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 16:56:47 ON 04 APR 2007
L4             25 S L3/P
                  E US20050238724/PN,PRN,AN
L5              0 S E3/RN
L6              1 S E3

     FILE 'REGISTRY' ENTERED AT 16:58:38 ON 04 APR 2007
L7              0 S L6

     FILE 'HCAPLUS' ENTERED AT 17:00:04 ON 04 APR 2007
                  E LAMOTRIGINE+ALL/CT
                  S LAMOTRIGINE/CN

     FILE 'REGISTRY' ENTERED AT 17:00:26 ON 04 APR 2007
L8              1 S LAMOTRIGINE/CN

     FILE 'HCAPLUS' ENTERED AT 17:00:27 ON 04 APR 2007
L9           1265 S L8
L10            27 S "3,5-DIAMINO-6-(2,3-DICHLOROPHENYL)-1,2,4-TRIAZINE"

     FILE 'REGISTRY' ENTERED AT 17:02:26 ON 04 APR 2007
L11             1 S 84057-84-1/RN

     FILE 'HCAPLUS' ENTERED AT 17:02:48 ON 04 APR 2007
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L13        111187 S L10 OR L12  AND PARTICLE OR GRANULE
L14             0 S L12 (N) PARTICLE
L15             0 S L12 (W) PARTICLE
L16            46 S L12 AND CNS
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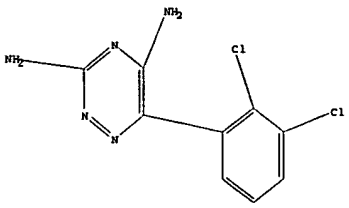

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 9 TO ITERATE

100.0% PROCESSED 9 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 9 TO 360
PROJECTED ANSWERS: 3 TO 163

L2 3 SEA SSS SAM L1

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'ABS' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual fields or predefined formats. The predefined substance formats are: (RN = CAS Registry Number)

REG - RN
SAM - Index Name, MF, and structure - no RN
FIDE - All substance data, except sequence data
IDE - FIDE, but only 50 names
SQIDE - IDE, plus sequence data
SQIDE3 - Same as SQIDE, but 3-letter amino acid codes are used
SQD - Protein sequence data, includes RN

SQD3 - Same as SQD, but 3-letter amino acid codes are used
SQN - Protein sequence name information, includes RN

CALC - Table of calculated properties
EPROP - Table of experimental properties
PROP - EPROP and CALC

Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ABS -- Abstract
APPS -- Application and Priority Information
BIB -- CA Accession Number, plus Bibliographic Data
CAN -- CA Accession Number
CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
IND -- Index Data
IPC -- International Patent Classification
PATS -- PI, SO
STD -- BIB, IPC, and NCL

IABS -- ABS, indented, with text labels
IBIB -- BIB, indented, with text labels
ISTD -- STD format, indented

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

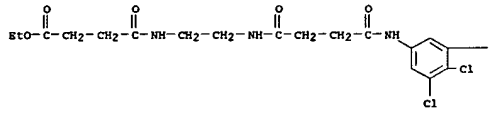
The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available.
The MAX format is the same as ALL.
The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

For additional information, please consult the following help messages:

HELP DFIELDS -- To see a complete list of individual display fields.
HELP FORMATS -- To see detailed descriptions of the predefined formats.
ENTER DISPLAY FORMAT (IDE):ide

L2 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2007 ACS on STN
RN 865316-75-6 REGISTRY
ED Entered STN: 23 May 2006
CN Butanoic acid, 4-[[2-[[4-[[3,4-dichloro-5-(3,5-diamino-1,2,4-triazin-6-yl)phenyl]amino]-1,4-dioxobutyl]amino]ethyl]amino]-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)
MF C21 H26 Cl2 N8 O5
SR CA
LC STN Files: CA, CAPLUS

PAGE 1-A



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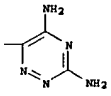

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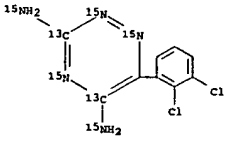
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2007 ACS on STN
RN 478189-71-8 REGISTRY
ED Entered STN: 06 Jan 2003
CN 1,2,4-Triazine-3,5-diamine-3,5-13C2-N,N',1,2,4-15N5, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)
MF C9 H7 Cl2 N5
SR CA
LC STN Files: CA, CAPLUS, CASREACT



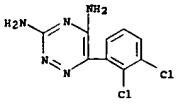
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2007 ACS on STN
RN 454695-04-6 REGISTRY
ED Entered STN: 25 Sep 2002
CN Formamide, N,N-dimethyl-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-

triazine-3,5-diamine (3:2) (9CI) (CA INDEX NAME)
MF C9 H7 Cl2 N5 . 3/2 C3 H7 N O
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

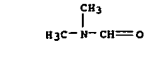
CM 1

CRN 84057-84-1
CMF C9 H7 Cl2 N5



CM 2

CRN 68-12-2
CMF C3 H7 N O



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s l1 sss full
FULL SEARCH INITIATED 16:56:39 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 212 TO ITERATE

100.0% PROCESSED 212 ITERATIONS 128 ANSWERS
SEARCH TIME: 00.00.01

L3 128 SEA SSS FUL L1

=> fil hcaplus
COST IN U.S. DOLLARS SINCE FILE ENTRY 178.40 TOTAL SESSION 178.61

FULL ESTIMATED COST

FILE 'HCAPLUS' ENTERED AT 16:56:47 ON 04 APR 2007
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FILE COVERS 1907 - 4 Apr 2007 VOL 146 ISS 15
FILE LAST UPDATED: 3 Apr 2007 (20070403/ED)

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=> d his

(FILE 'HOME' ENTERED AT 16:55:13 ON 04 APR 2007)

FILE 'REGISTRY' ENTERED AT 16:55:37 ON 04 APR 2007
L1 STRUCTURE UPLOADED
L2 3 S L1 SSS SAM
L3 128 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 16:56:47 ON 04 APR 2007

=> s l3/p
L4 25 L3/P

=> d l4 1-25 ibib abs

L4 ANSWER 1 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:411970 HCAPLUS
DOCUMENT NUMBER: 144:425648
TITLE: Lamotrigine analogs for production of anti-lamotrigine antibodies and use as immunoassay reagents
INVENTOR(S): Ouyang, Anlong; Arabshahi, Lili; Roberts, Mark; Wall, Melissa
PATENT ASSIGNEE(S): Seradyn, Inc., USA
SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006047372	A2	20060504	WO 2005-US38100	20051021
WO 2006047372	A3	20060727		
WO 2006047372	A9	20061005		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2006115865	A1	20060601	US 2005-254650	20051020
PRIORITY APPLN. INFO.:			US 2004-621764P	P 20041025
			US 2005-254650	A 20051020

OTHER SOURCE(S): MARPAT 144:425648
AB The invention discloses lamotrigine analogs that have substituents at the triazine 3-position and on the benzene 4-position and 5-position. The lamotrigine analogs can include immunogenic moieties that can be used to prepare anti-lamotrigine antibodies, or antigenic moieties that can be used in immunodiagnostic assays for lamotrigine. Also, the lamotrigine analog can include tracer moieties for detecting the presence or amount of the analog during an immunodiagnostic assay. Addnl., the lamotrigine analogs can be used in immunodiagnostic assays to compete with lamotrigine for binding with anti-lamotrigine antibodies. Lamotrigine analog preparation is described.

L4 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:411913 HCAPLUS
DOCUMENT NUMBER: 144:425647
TITLE: Immunoassays for lamotrigine
INVENTOR(S): Ouyang, Anlong; Arabshahi, Lili; Roberts, Mark; Wall, Melissa
PATENT ASSIGNEE(S): Seradyn, Inc., USA
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006047451	A2	20060504	WO 2005-US38258	20051021

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2006172356	A1	20060803	US 2005-254637	20051020
PRIORITY APPLN. INFO.:			US 2004-621764P	P 20041025
			US 2005-254637	A 20051020

OTHER SOURCE(S): MARPAT 144:425647
AB Generally, the present invention relates to lamotrigine analogs that have substituents at the triazine 3-position and on the benzene 4-position and 5-position. The lamotrigine analogs can include immunogenic moieties that can be used to prepare anti-lamotrigine antibodies, or antigenic moieties that can be used in immunodiagnostic assays for lamotrigine. Also, the lamotrigine analog can include tracer moieties for detecting the presence

or amount of the analog during an immunodiagnostic assay. Addnl., the lamotrigine analogs can be used in immunodiagnostic assays to compete with lamotrigine for binding with anti-lamotrigine antibodies.

L4 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1010006 HCAPLUS
DOCUMENT NUMBER: 144:312050
TITLE: A new approach to the synthesis of lamotrigine and other 3,5-diamino-1,2,4-triazine derivatives
AUTHOR(S): Ulomskii, E. N.; Shestakova, T. S.; Deev, S. L.; Rusinov, V. L.; Chupakhin, O. N.
CORPORATE SOURCE: Ural State Technical University, Yekaterinburg, 620002, Russia
SOURCE: Russian Chemical Bulletin (2005), 54(3), 726-732
CODEN: RCBUEY; ISSN: 1066-5285
PUBLISHER: Springer Science+Business Media, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new in principle method for the synthesis of 6-aryl(hetaryl)-3,5-diamino-1,2,4-triazines by decomposition of pre-synthesized tetrazolo[1,5-b][1,2,4]triazines was developed. The advantages of this method over traditional methods were demonstrated using the synthesis of a modern antiepileptic preparation lamotrigine, as an example. The crystal structure of 6-phenyltetrazolo[1,5-b][1,2,4]triazin-7-amine is presented (monoclinic, space group P21/c, a 10.935(2), b 6.7330(10), c 13.279(3) Å, β 93.20(3)°, V 976.1(3) Å3, Z 4).
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:421792 HCAPLUS
DOCUMENT NUMBER: 142:430313
TITLE: Process for preparation of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (Lamotrigine) via reaction of 2,3-dichlorobenzoyl chloride with cuprous cyanide and then with aminoguanidine bicarbonate followed by cyclization.
INVENTOR(S): Vyas, Sharad Kumar
PATENT ASSIGNEE(S): Torrent Pharmaceuticals Ltd., India
SOURCE: Indian, 12 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 183150	A1	19990925	IN 1998-CA2171	19981214
CA 2334937	A1	20000622	CA 1999-2334937	19991207
CA 2334937	C	20040921		
WO 2000035888	A1	20000622	WO 1999-IB1955	19991207

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,

CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2000012924	A	20000703	AU 2000-12924	19991207
EP 1140872	A1	20011010	EP 1999-956293	19991207
EP 1140872	B1	20030917		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

AT 250041	T	20031015	AT 1999-956293	19991207
RU 2231526	C2	20040627	RU 2001-115698	19991207
US 6111101	A	20000829	US 1999-456501	19991208
PRIORITY APPLN. INFO.:			IN 1998-CA2171	A 19981214
			WO 1999-IB1955	W 19991207

OTHER SOURCE(S): CASREACT 142:430313
AB Lamotrigine was prepared by reaction of 2,3-dichlorobenzoyl chloride with CuCN (1:1-2 molar ratio) in MeCN and a cosolvent to produce dichlorobenzoyl cyanide, reaction of the latter with aminoguanidine bicarbonate to produce the cyanoimine intermediate 2-[cyano(2,3-dichlorophenyl)methylene]hydrazinecarboximidamide, and cyclization of this in the presence of aqueous KOH at 80°-reflux.

L4 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:421470 HCAPLUS
DOCUMENT NUMBER: 141:7119
TITLE: Preparation of crystalline lamotrigine and its monohydrate
INVENTOR(S): Manjunatha, Sulur G.; Kulkarni, Ashok Krishna; Kishore, Charugundla; Bokka, Ravisankar
PATENT ASSIGNEE(S): Jubilant Organosys Limited, India
SOURCE: Brit. UK Pat. Appl., 25 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2395483	A	20040526	GB 2003-15608	20030703
WO 2005003104	A2	20050113	WO 2004-IN186	20040628
WO 2005003104	A3	20050922		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:			GB 2003-15608	A 20030703

OTHER SOURCE(S): CASREACT 141:7119
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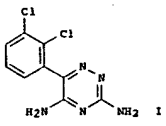

I

AB The invention relates to crystalline lamotrigine (3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine) (I) monohydrate and anhydrous lamotrigine. An improved process for manufacturing these products comprises reacting 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in aqueous mineral acid, optionally together with a water miscible organic solvent, at 30-80° to produce the 2-(2,3-dichlorophenyl)-2-(guanidinylimino)acetonitrile (Schiff base) (II). The Schiff base II is further cyclized in aqueous organic solvent, e.g. alc. to produce pure lamotrigine of a pharmaceutically acceptable quality which on further drying at 45-50° under vacuum yields lamotrigine monohydrate, and/or on further drying at 100-110° yields anhydrous lamotrigine. The lamotrigine monohydrate or anhydrous lamotrigine thereby produced may then be brought into association with a pharmaceutically acceptable carrier for administration to a patient in need thereof.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:390214 HCAPLUS
DOCUMENT NUMBER: 140:391299
TITLE: Process for preparing 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile and a process for its cyclization into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine
INVENTOR(S): Dalmases Barjoan, Pere; Bessa Bellmunt, Jordi
PATENT ASSIGNEE(S): Laboratorios Vita, S.A., Spain
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039767	A1	20040513	WO 2003-IB4763	20031027
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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ES 2209639	A1	20040616	ES 2002-2502	20021031

ES 2209639	B1	20050801		
AU 2003272019	A1	20040525	AU 2003-272019	20031027
EP 1556341	A1	20050727	EP 2003-753860	20031027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006052625	A1	20060309	US 2005-532397	20050422
US 7179913	B2	20070220		
NO 2005002574	A	20050527	NO 2005-2574	20050527
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			WO 2003-IB4763 W	20031027

OTHER SOURCE(S): CASREACT 140:391299
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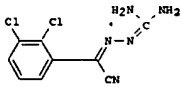

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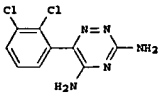


II

AB A method for preparing the intermediate 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile (I; m.p. 180-183°) which comprises the condensation reaction of 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in a non-aqueous medium in the presence of methanesulfonic acid, which produces good I yields and short reaction times. I is cyclized into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (II; m.p. 217°) under reflux in an aliph alc. (e.g., ethanol) or alc.-water mixture
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:267313 HCAPLUS
DOCUMENT NUMBER: 140:303705
TITLE: Two-step process for the synthesis of high-purity 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine from 2,3-dichlorobenzoyl cyanide and aminoguanidine dimesylate

INVENTOR(S): Neu, Jozsef; Gizur, Tibor; Toerley, Jozsef; Csabai, Janos; Vegh, Ferenc; Kalvin, Peter; Tarkanyi, Gabor
PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026845	A1	20040401	WO 2003-HU72	20030918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
HU 200203114	A2	20040528	HU 2002-3114	20020920
CA 2498761	A1	20040401	CA 2003-2498761	20030918
AU 2003267676	A1	20040408	AU 2003-267676	20030918
EP 1539720	A1	20050615	EP 2003-748368	20030918
EP 1539720	B1	20061122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 346051	T	20061215	AT 2003-748368	20030918
IN 2005KN00267	A	20060714	IN 2005-KN267	20050224
US 2006178511	A1	20060810	US 2005-528379	20051129
PRIORITY APPLN. INFO.:			HU 2002-3114 A	20020920
			WO 2003-HU72 W	20030918

OTHER SOURCE(S): CASREACT 140:303705
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

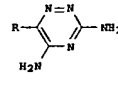
AB High-purity 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (I; i.e., lamotrigine) is prepared by the condensation reaction of 2,3-dichlorobenzoyl cyanide (II) with 1-2 mol equivalent of an aminoguanidine salt (e.g., aminoguanidine dimesylate) in 3-6 mol equivalent of methanesulfonic acid, then the obtained adduct (III) is transformed without isolation into the desired product by contacting it with magnesium oxide, followed by crystallization of the product from an appropriate organic solvent (e.g., acetone).
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:507707 HCAPLUS
DOCUMENT NUMBER: 139:69292
TITLE: Process for the preparation of lamotrigine and related 3,5-diamino-6-substituted-1,2,4-triazines via

cyclization of cyanoiminoguanidines.
INVENTOR(S): Guntoori, Bhaskar Reddy; Che, Daqing; Murthy, K. S. Keshava
PATENT ASSIGNEE(S): Brantford Chemicals Inc., Can.
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6586593	B1	20030701	US 2002-46383	20020116
CA 2366521	A1	20030624	CA 2001-2366521	20011224
CA 2366521	C	20070306		
WO 2003078407	A1	20030925	WO 2002-CA1926	20021218
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002367765	A1	20030929	AU 2002-367765	20021218
EP 1458692	A1	20040922	EP 2002-807048	20021218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
NZ 533734	A	20051223	NZ 2002-533734	20021218
PRIORITY APPLN. INFO.:			CA 2001-2366521 A	20011224
			WO 2002-CA1926 W	20021218

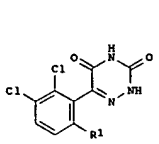
OTHER SOURCE(S): CASREACT 139:69292; MARPAT 139:69292
GI



I

AB Title compds. [I; R = (substituted) alkyl, aryl], were prepared by reaction of RCOCN with aminoguanidine in the presence of an organic sulfonic acid in an organic solvent under anhydrous conditions to give (HO)C(R)(CN)NHNC(NH2)2, dehydration of this to give NCC(R){:NN:C(NH2)2}, and cyclization of the latter. Thus, aminoguanidine hydrochloride in DMF was treated with MeSO3H and 2,3-dichlorobenzoyl chloride followed by stirring for 1 h, addition of SOCl2, and stirring for 1 h to give 39.2% iminoguanidine derivative The latter was refluxed with KOH in Me2CHOH to give 82% lamotrigine monohydrate.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:385795 HCAPLUS
DOCUMENT NUMBER: 140:199296
TITLE: Synthesis of oxo analogs of Lamotrigine and related compounds
AUTHOR(S): Hlavac, Jan; Buchtik, Roman; Slouka, Jan; Hradil, Pavel; Wiedermannova, Iveta
CORPORATE SOURCE: Department of Organic Chemistry, Palacky University, Olomouc, CZ-771 46, Czech Rep.
SOURCE: ARKIVOC (Gainesville, FL, United States) (2003), (1), 22-28
CODEN: AGFUAR
URL: http://www.arkat-usa.org/ark/journal/2003/General/2-556F/556F.pdf
PUBLISHER: Arkat USA Inc.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 140:199296
GI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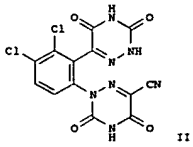

II

AB Lamotrigine oxo analogs I (R1 = H, Cl, Br, iodo, HO) were prepared from azauracil I (R1 = NH2) via the formation of the intermediate diazonium salt. Coupling of this diazonium salt with Et cyanoacetylcarbamate gave the corresponding carbamoyl hydrazone, which underwent intramol. cyclization upon reflux in pyridine to afford bis(triazinyl)benzene II containing two 6-azauracil rings.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:334829 HCAPLUS
DOCUMENT NUMBER: 138:343889
TITLE: Novel pharmaceutical compounds containing drugs bound to polypeptides
INVENTOR(S): Picariello, Thomas
PATENT ASSIGNEE(S): New River Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 4662 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 24
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2003034980	A2	20030501	WO 2001-US43089	20011114
WO 2003034980	A8	20051103		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2428971	A1	20030501	CA 2001-2428971	20011114
EP 1401374	A1	20040331	EP 2001-274606	20011114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2006516948	T	20060713	JP 2003-537549	20011114
US 2004063628	A1	20040401	US 2002-156527	20020529
US 7060708	B2	20060613		
US 2007060500	A1	20070315	US 2006-392878	20060330
PRIORITY APPLN. INFO.:			US 2000-274622P	P 20001114
			US 1999-265415	B2 19990310
			US 1999-411238	B2 19991004
			WO 2000-US5693	A 20000306
			US 2000-642820	A2 20000822
			US 2000-247594P	P 20001114
			US 2000-247622P	P 20001114
			US 2000-247684P	P 20001114
			US 2000-248528P	P 20001116
			US 2000-248620P	P 20001116
			US 2000-248659P	P 20001116
			US 2000-248660P	P 20001116
			US 2000-248662P	P 20001116
			US 2000-248663P	P 20001116
			US 2000-248685P	P 20001116
			US 2000-248733P	P 20001116
			US 2000-248737P	P 20001116
			US 2000-248738P	P 20001116
			US 2000-248748P	P 20001116
			US 2000-248764P	P 20001116
			US 2000-248767P	P 20001116
			US 2000-248768P	P 20001116
			US 2000-248769P	P 20001116
			US 2000-248770P	P 20001116
			US 2000-248771P	P 20001116
			US 2000-248772P	P 20001116
			US 2000-248774P	P 20001116
			US 2000-248776P	P 20001116
			US 2000-248777P	P 20001116
			US 2000-248778P	P 20001116
			US 2000-248779P	P 20001116
			US 2000-248782P	P 20001116
			US 2000-248787P	P 20001116
			US 2000-248794P	P 20001116
			US 2000-248795P	P 20001116
			US 2000-248796P	P 20001116
			US 2000-248797P	P 20001116
			US 2001-933708	A2 20010822

			US 2001-986426	A2 20011108
			US 2001-987458	B2 20011114
			WO 2001-US43089	W 20011114
			US 2001-988034	B2 20011116
			US 2001-988071	B2 20011116
			WO 2001-US43115	B2 20011116
			WO 2001-US43117	B2 20011116
			US 2002-358381P	P 20020222
			US 2002-366258P	P 20020322
			US 2002-156527	A2 20020529
			US 2003-507012P	P 20030930
			US 2004-567800P	P 20040505
			US 2004-567802P	P 20040505
			US 2004-568011P	P 20040505
			US 2004-923088	A2 20040823
			WO 2004-US32131	A2 20040930

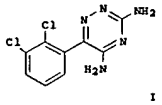
AB Compns. comprising polypeptides and drugs covalently attached to the polypeptide are disclosed. Also provided is a method for delivery of these drugs to a patient comprising administering to the patient a composition comprising a polypeptide and a drug covalently attached to the polypeptide. Also provided is a method for protecting drugs from degradation comprising covalently attaching them to a polypeptide. Also provided is a method for controlling release of drugs from a composition comprising covalently attaching them to the polypeptide.

L4 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:76761 HCAPLUS
DOCUMENT NUMBER: 138:137336
TITLE: Method for producing lamotrigine from alpha-oxo-2,3-dichlorophenylacetamidinoaminoguanidino hydrazone by ring closure reaction
INVENTOR(S): Schneider, Geza; Gegoe, Csaba Lehel; Ondi, Levente; Mate, Attila Gergely; Lukacs, Ferenc; Nyerges, Miklos; Garaczi, Sandor
PATENT ASSIGNEE(S): Helm AG, Germany; CF Pharma Gyogyszergyarto Kft.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008393	A1	20030130	WO 2002-EP7433	20020704
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10134980	A1	20030213	DE 2001-10134980	20010717
DE 10134980	C2	20030528		
EP 1311492	A1	20030521	EP 2002-758308	20020704
EP 1311492	B1	20040908		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, BG, CZ, EE				
CA 2417435	C	20040113	CA 2002-2417435	20020704
CA 2417435	A1	20030130		
ES 2224074	T3	20050301	ES 2002-2758308	20020704
US 2003191310	A1	20031009	US 2003-343225	20030515
US 6683182	B2	20040127		
PRIORITY APPLN. INFO.:			DE 2001-10134980	A 20010717
			WO 2002-EP7433	W 20020704

OTHER SOURCE(S): CASREACT 138:137336; MARPAT 138:137336
GI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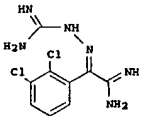
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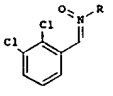
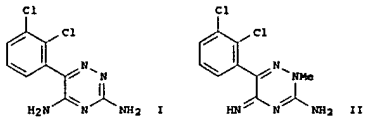

III

AB The invention relates to a method for producing 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine [lamotrigine (I)], or its pharmaceutically acceptable salts, by ring closure reaction from α-oxo-2,3-dichlorophenylacetamidinoaminoguanidino hydrazone (II) or its salts. The preparation of II from N-oxides, III [R = linear, branched or cyclic (un)substituted alkyl, aryl, aralkyl], or their salts, are also described. Thus, I was prepared from 2,3-Cl2C6H3CH:N(O)Ph, via cyanation with NaCN, amination to the acetamidine hydrochloride, reaction with aminoguanine bicarbonate to give II·HCl, treatment with aqueous NaOH to give the free base, which is cyclized to I; cyclization of II·HCl gives I·HCl.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:549382 HCAPLUS
DOCUMENT NUMBER: 138:24695
TITLE: Synthesis of stable isotopically labelled versions of Lamotrigine and its methylated metabolite
AUTHOR(S): Manning, Calvin O.; Wadsworth, Alan H.; Fellows, Ian

CORPORATE SOURCE: Chemical Development, GlaxoSmithKline Research and Development, Stevenage, SG1 2NY, UK
SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals (2002), 45(7), 611-618
CODEN: JLCRD4; ISSN: 0362-4803
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:24695
GI

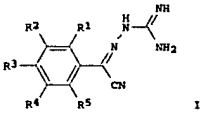


AB Lamotrigine (I) is a sodium channel antagonist used for the treatment of epilepsy. Stable isotopically labeled [M + 7] analogs of I and of its N-methylated metabolite II were prepared using [M + 5] labeled [13C, 15N4]-aminoguanidine, obtained from labeled thiourea. The overall yield for isotopically labeled II was 34% from [M + 3] labeled [13C, 15N2]-thiourea.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:631908 HCAPLUS
DOCUMENT NUMBER: 135:195578
TITLE: Process for preparing substituted benzoyl cyanide amidinohydrazones as intermediates for synthesis of 3,5-diamino-6-phenyl-1,2,4-triazines
INVENTOR(S): Nadaka, Vladimir; Lexner, Jael; Kaspi, Joseph
PATENT ASSIGNEE(S): Chemagis Ltd., Israel
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1127873	A2	20010829	EP 2001-103660	20010223
EP 1127873	A3	20030507		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
IL 134730	A	20031031	IL 2000-134730	20000225
CA 2337280	A1	20010825	CA 2001-2337280	20010215
HU 200100740	A2	20011128	HU 2001-740	20010215
US 2001025118	A1	20010927	US 2001-789634	20010222
US 6329521	B2	20011211		

PRIORITY APPLN. INFO.: IL 2000-134730 A 20000225
OTHER SOURCE(S): CASREACT 135:195578; MARPAT 135:195578
GI



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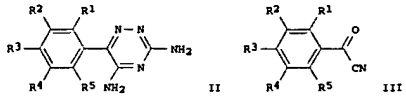


II III

AB The title compds. [I; R1-R5 = H, halo, alkyl, etc.], useful as intermediates for synthesis of 1,2,4-triazines II (active in the treatment of CNS disorders), were prepared by reacting the benzoyl cyanides III with aminoguanidine bicarbonate in a mixture of a water-soluble solvent and polyphosphoric acid. Thus, reacting 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in the presence of polyphosphoric acid in MeCN afforded 2,3-dichlorobenzoyl cyanide amidinohydrazone which was then heated under reflux in PrOH to give 2,3-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine.

L4 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:507682 HCAPLUS
DOCUMENT NUMBER: 135:108812
TITLE: Preparation of 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (lamotrigine)
INVENTOR(S): Radhakrishnan, Tarur Venkatasubramanian; Sasikumar, Thoovara Mohan; Srivastava, Anita Ranjan
PATENT ASSIGNEE(S): RPG Life Sciences Limited, India
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001049669	A1	20010712	WO 2000-IN1	20000103
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,				

SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

GB 2372988	A	20020911	GB 2002-14791	20000103
GB 2372988	B	20040407		
BR 2000016980	A	20021001	BR 2000-16980	20000103
DE 10085384	T0	20021212	DE 2000-10085384	20000103
DE 10085384	B4	20060614		
AU 763244	B2	20030717	AU 2000-44288	20000103
IN 2002MN00829	A	20040313	IN 2002-MN829	20020619
US 6639072	B1	20031028	US 2002-149429	20020624

PRIORITY APPLN. INFO.: WO 2000-IN1 A 20000103
AB The title compound was prepared by hydrogenation of 2,3-Cl2C6H3NO2 in MeOH at 80 psi H pressure using Raney Ni catalyst at 30° to give 2,3-Cl2C6H3NH2 which was diazotized and converted to nitrile with CuCN/NaCN at 65-70°. The resulting 2,3-Cl2C6H3CN was hydrolyzed to give 2,3-Cl2C6H3CO2 which was converted to acid chloride at 80° with SOCl2. The 2,3-Cl2C6H3COCl was cyano-dehalogenated with CuCN/KI by refluxing in PhCl under an inert atmospheric and the product 2,3-Cl2C6H3COCN was condensed with aminoguanidine bicarbonate in PhMe in the presence of H2SO4 and p-MeC6H4SO3H at 100-120°, followed by in-situ cyclization of the Schiff base by refluxing with MeONa in MeOH. Crude lamotrigine is purified by recrystn. from MeOH.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:369058 HCAPLUS
DOCUMENT NUMBER: 136:14957
TITLE: Isolation of lamotrigine 2-N-glucuronide from guinea pig urine
AUTHOR(S): Yeh, Shih-Woei; Yu, Hsiu-Ying
CORPORATE SOURCE: School of Pharmacy, National Taiwan University, Taipei, 100, Taiwan
SOURCE: Chinese Pharmaceutical Journal (Taipei, Taiwan) (2000), 52(5), 241-249
CODEN: CPHJEP; ISSN: 1016-1015
PUBLISHER: Pharmaceutical Society of Republic of China
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lamotrigine (LT) is a novel anticonvulsant. Its major metabolite in human is 2-N-glucuronide (LT-2NG). In order to investigate the metabolic characteristics of LT in our laboratory, a reference standard of LT-2NG was required.
The purpose of this experiment was to isolate pure LT-2NG from the urine of LT-treated guinea pigs. The pooled urine of guinea pigs fed with LT was eluted with methanol through XAD-2 column. LT-2NG in the eluent was purified by semi-preparative HPLC equipped with a C8 column and a UV detector set at 267 nm. The mobile phase for HPLC was 0.01M ammonium acetate (pH 6.6) containing 12% of methanol. The isolated LT-2NG was confirmed by mass, 1H NMR and 13C NMR spectroscopic anal. The mol. ion 432.1, a downfield anomeric proton at 5.39 ppm, and an upfield shift (-6.9 ppm) of the triazine ring C-3 indicate attachment of the glucuronide to the N-2 of LT. These spectra were identical with the reported spectra of LT-2NG isolated from human urine.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:421116 HCAPLUS
DOCUMENT NUMBER: 133:60362
TITLE: An improved process for preparation of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine
INVENTOR(S): Vyas, Sharad Kumar
PATENT ASSIGNEE(S): India
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035888	A1	20000622	WO 1999-IB1955	19991207
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IN 183150	A1	19990925	IN 1998-CA2171	19981214
CA 2334937	A1	20000622	CA 1999-2334937	19991207
CA 2334937	C	20040921		
AU 2000012924	A	20000703	AU 2000-12924	19991207
EP 1140872	A1	20011010	EP 1999-956293	19991207
EP 1140872	B1	20030917		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 250041	T	20031015	AT 1999-956293	19991207
RU 2231526	C2	20040627	RU 2001-115698	19991207
			IN 1998-CA2171 A	19981214
			WO 1999-IB1955 W	19991207

PRIORITY APPLN. INFO.:
AB 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (lamotrigine) (I) useful as antiepileptic drug (no data) is prepared in a 3 step process. Thus, 2,3-dichlorobenzoylchloride was treated with cuprous cyanide in presence of acetonitrile and a solvent to produce 2,3-dichlorobenzoyl cyanide, further with aminoguanidine and cyclized to produce I.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:795469 HCAPLUS
DOCUMENT NUMBER: 132:26963
TITLE: Preparation of 1,2,4-triazine derivative, and its use as reference marker for testing purity and stability of lamotrigine
INVENTOR(S): Edmeades, Lorraine Mary; Griffith-Skinner, Nigel Arthur; Hill, Derek Anthony; Hill, Graham Thornton; Packham, Terrence William
PATENT ASSIGNEE(S): The Wellcome Foundation Limited, UK
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 963980	A2	19991215	EP 1999-200695	19990310
EP 963980	A3	20000531		
EP 963980	B1	20020605		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
SG 85628	A1	20020115	SG 1999-1252	19990225
MX 9902202	A	20000831	MX 1999-2202	19990305
KR 2000005611	A	20000125	KR 1999-7632	19990309
HR 990074	A1	20001031	HR 1999-74	19990309
ZA 9901951	A	19990816	ZA 1999-1951	19990310
JP 2989189	B2	19991213	JP 1999-63792	19990310
JP 2000009714	A	20000114		
NO 9901151	A	19991213	NO 1999-1151	19990310
CN 1238454	A	19991215	CN 1999-103445	19990310
AU 9920319	A	20000106	AU 1999-20319	19990310
TR 9900520	A2	20000121	TR 1999-520	19990310
HU 9900592	A2	20000428	HU 1999-592	19990310
BR 9900984	A	20000502	BR 1999-984	19990310
NZ 334590	A	20000728	NZ 1999-334590	19990310
CA 2265194	C	20001010	CA 1999-2265194	19990310
US 6333198	B1	20011225	US 1999-265670	19990310
EP 1170588	A1	20020109	EP 2001-203376	19990310
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 218552	T	20020615	AT 1999-200695	19990310
PT 963980	T	20021031	PT 1999-200695	19990310
ES 2178342	T3	20021216	ES 1999-200695	19990310
CN 1306210	A	20010801	CN 2000-122208	20000725
US 2002055177	A1	20020509	US 2001-940422	20010829
NO 2003002753	A	19991213	NO 2003-2753	20030617

PRIORITY APPLN. INFO.:
GB 1998-12413 A 19980610
EP 1999-200695 A3 19990310
US 1999-265670 A3 19990310

AB A method of testing the purity or stability to degradation of a sample of lamotrigine or a pharmaceutical dosage form comprising lamotrigine consists of assaying the sample for the presence of a compound selected from 3-amino-6-(2,3-dichlorophenyl)-1,2,4-triazine-5-(4H)-one and N-[5-amino-6-(2,3-dichlorophenyl)-1,2,4-triazine-3-yl]-2,3-dichlorobenzamide (I). A process for producing compound I, is also disclosed. Lamotrigine was treated with 2,3-dichlorobenzoyl chloride to give I. TLC-densitometry was used to determine I in lamotrigine tablets.

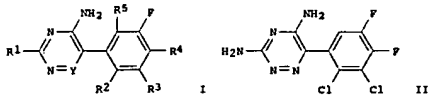
L4 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:473716 HCAPLUS
DOCUMENT NUMBER: 127:81468
TITLE: Fluorophenyl-triazine and pyrimidine derivatives as compounds acting on the central nervous system
INVENTOR(S): Torrens Jover, Antoni; Frigola Constansa, Jordi
PATENT ASSIGNEE(S): Laboratorios Del Dr. Esteve, S.A., Spain; Torrens Jover, Antoni; Frigola Constansa, Jordi
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9720827	A1	19970612	WO 1996-EP5593	19961204
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2741879	A1	19970606	FR 1995-14354	19951205
AU 9711943	A	19970627	AU 1997-11943	19961204
ES 2128960	A1	19990516	ES 1996-2667	19961205
ES 2128960	B1	20000116		

PRIORITY APPLN. INFO.:
FR 1995-14354 A 19951205
WO 1996-EP5593 W 19961204

OTHER SOURCE(S): CASREACT 127:81468; MARPAT 127:81468
GI



AB Novel fluorophenyl-triazine and pyrimidine derivs. I and their physiol. acceptable salts are disclosed [wherein R1 = amino, 1-piperazinyl or 4-alkylpiperazin-1-yl, where alkyl = C1-4 chain, preferably Me; R2, R3, R4 = halo, preferably F or Cl; R5 = H or halo, preferably F or Cl; Y = N, CH]. A method for preparing the compds. is also disclosed, as are pharmaceutical compns. containing a pharmaceutically acceptable carrier and at least one such compound The compds. are CNS agents which act by inhibiting the release of glutamate. Examples include 13 syntheses, 1 standard formulation, and biol. data for 5 compds. For instance, 2,3-dichloro-4,5-difluorobenzoic acid (prepared in 3 steps) was converted to the acid chloride (99%) and then to the acyl cyanide (98%), and the latter was condensed with aminoguanidine bicarbonate and cyclized (31%) to give title compound II. In a test for prevention of hypoxic death in mice, II had an ED50 of 0.6 mg/kg i.p., vs. 1.2 mg/kg for lamotrigine.

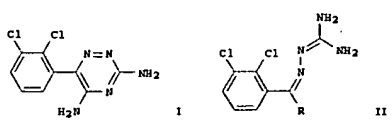
L4 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:548552 HCAPLUS
DOCUMENT NUMBER: 125:195694
TITLE: Preparation of lamotrigine.
INVENTOR(S): Winter, Raymond Geoffrey; Sawyer, David Alan; Germain, Andrew
PATENT ASSIGNEE(S): Wellcome Foundation Limited, UK
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9620934	A1	19960711	WO 1995-GB3048	19951229
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9643115	A	19960724	AU 1996-43115	19951229
EP 800520	A1	19971015	EP 1995-941817	19951229
EP 800520	B1	20020619		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
HU 77346	A2	19980330	HU 1997-1867	19951229
HU 224688	B1	20051228		
JP 11501007	T	19990126	JP 1995-520803	19951229
RU 2145602	C1	20000220	RU 1997-112881	19951229
AT 219467	T	20020715	AT 1995-941817	19951229
PT 800520	T	20021129	PT 1995-941817	19951229
ES 2177672	T3	20021216	ES 1995-941817	19951229
FI 9702719	A	19970827	FI 1997-2719	19970624
US 5912345	A	19990615	US 1997-836153	19970625

PRIORITY APPLN. INFO.:
GB 1994-26439 A 19941230
GB 1994-26447 A 19941230
WO 1995-GB3048 W 19951229

OTHER SOURCE(S): CASREACT 125:195694; MARPAT 125:195694
GI



AB Lamotrigine (I) was prepared by irradiation of (II; R = CN, CONH2) with UV or visible radiation in an organic solvent, or, when R = CN, by heating. Thus, II (R = CN) was refluxed in 1-propanol under irradiation from a medium pressure Hg lamp for 8 h to give 73% lamotrigine.

L4 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:546365 HCAPLUS
DOCUMENT NUMBER: 125:195693
TITLE: Preparation of lamotrigine.
INVENTOR(S): Lee, Grahame Roy
PATENT ASSIGNEE(S): Wellcome Foundation Limited, UK
SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9620935	A1	19960711	WO 1995-GB3049	19951229
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9643116	A	19960724	AU 1996-43116	19951229
EP 800521	A1	19971015	EP 1995-941818	19951229
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
HU 77347	A2	19980330	HU 1997-1875	19951229
JP 11507011	T	19990622	JP 1995-520618	19951229
RU 2162081	C2	20010120	RU 1997-112921	19951229
FI 9702720	A	19970827	FI 1997-2720	19970624
US 5925755	A	19990720	US 1997-836152	19970625

PRIORITY APPLN. INFO.:
GB 1994-26448 A 19941230
WO 1995-GB3049 W 19951229

AB Lamotrigine, 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (I), is prepared by treating 6-(2,3-dichlorophenyl)-5-chloro-3-thiomethyl-1,2,4-triazine (II) with NH3. Thus, II (preparation given) was heated with ethanolic NH3 in a sealed tube at 180° and 280 psi for 72 h to give I.

L4 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:128970 HCAPLUS
DOCUMENT NUMBER: 116:128970
TITLE: Preparation of 6-aminophenyl-3,5-diamino-1,2,4-triazines as neuroprotective agents
INVENTOR(S): Leach, Michael John; Nobbs, Malcolm Stuart
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 459829	A1	19911204	EP 1991-304962	19910531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 9104158	A	19930301	ZA 1991-4158	19910530
CA 2043642	A1	19911202	CA 1991-2043642	19910531
FI 9102622	A	19911202	FI 1991-2622	19910531
AU 9178099	A	19911205	AU 1991-78099	19910531
AU 630811	B2	19921105		
HU 60726	A2	19921028	HU 1991-1827	19910531
JP 06025193	A	19940201	JP 1991-235335	19910531

PRIORITY APPLN. INFO.:
GB 1990-12312 A 19900601

OTHER SOURCE(S): MARPAT 116:128970

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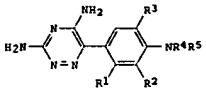

I

AB Title compds. (I; 1 of R1-R3 = Cl and the others = H or Cl; R4, R5 = H, alkyl) were prepared Thus, 2,5,3-Cl2(H2N)C6H2CO2H was converted in 3 steps to 2,3,5-Cl3C6H2COCN which was cyclocondensed with H2NC(:NH)NHNH2 and the product nitrated to give, after reduction, I (R1-R3 = Cl, R4 = R5 = H). The latter had IC50 of <10 μM against glutamate release from rat brain slices.

L4 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:112505 HCAPLUS
DOCUMENT NUMBER: 108:112505
TITLE: Preparation of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine isethionate as an antiepileptic
INVENTOR(S): Sawyer, David Alan; Copp, Frederick Charles
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 5 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 247892	A1	19871202	EP 1987-304776	19870529
EP 247892	B1	19910424		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DK 8702759	A	19871201	DK 1987-2759	19870529
DK 166278	B	19930329		
DK 166278	C	19930823		
FI 8702406	A	19871201	FI 1987-2406	19870529
FI 90770	B	19931215		
FI 90770	C	19940325		
AU 8773684	A	19871203	AU 1987-73684	19870529
AU 597982	B2	19900614		
JP 62289570	A	19871216	JP 1987-134772	19870529
JP 07051571	B	19950605		
HU 45978	A2	19880928	HU 1987-2487	19870529
HU 196769	B	19890130		
ZA 8703896	A	19890125	ZA 1987-3896	19870529
US 4847249	A	19890711	US 1987-56136	19870529
AT 62902	T	19910515	AT 1987-304776	19870529
CA 1286670	C	19910723	CA 1987-538395	19870529
IL 82710	A	19920115	IL 1987-82710	19870529
PRIORITY APPLN. INFO.:			GB 1986-13183 A	19860530
			EP 1987-304776 A	19870529

AB The title compound (I.isethionate), useful as an anticonvulsant (no data),

was prepared by reaction of I with 2-hydroxyethanesulfonic acid (II) or by reaction of I salts with the anion of II. A 1.0 M solution of Na isethionate in H2O was passed through a column of IR 120 (H) ion exchange resin. I (preparation given) was added to the resulting II and the solution was filtered and evaporated Recrystn. from industrial methylated spirit gave 72% I.isethionate.

L4 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:542021 HCAPLUS
DOCUMENT NUMBER: 103:142021
TITLE: Triazine compounds having cardiovascular activity
INVENTOR(S): Allan, Geoffrey; Miller, Alastair Ainslie; Sawyer, David Alan
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 142306	A2	19850522	EP 1984-307374	19841026
EP 142306	A3	19861120		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4649139	A	19870310	US 1984-663682	19841022
DK 8405121	A	19850428	DK 1984-5121	19841026
FI 8404212	A	19850428	FI 1984-4212	19841026
AU 8434758	A	19850509	AU 1984-34758	19841026
AU 564667	B2	19870820		
JP 60109577	A	19850615	JP 1984-225636	19841026
DD 224033	A5	19850626	DD 1984-268757	19841026
HU 36102	A2	19850828	HU 1984-4003	19841026
HU 191566	B	19870330		
ES 537104	A1	19860416	ES 1984-537104	19841026
ZA 8408388	A	19860625	ZA 1984-8388	19841026
SU 1371500	A3	19880130	SU 1984-3805251	19841026
IL 73332	A	19880630	IL 1984-73332	19841026
PL 144899	B1	19880730	PL 1984-250213	19841026
CA 1261328	A1	19890926	CA 1984-466473	19841026
PRIORITY APPLN. INFO.:			GB 1983-28757 A	19831027
OTHER SOURCE(S):	MARPAT 103:142021			

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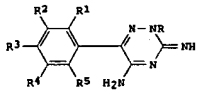


I

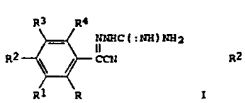
AB Tautomeric iminotriazinamines I [R = (un)substituted C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, C3-10 cycloalkyl; R1-R5 = H, halogen, alkenyloxy, acyl, acyloxy, cyano, NO2, aryl, alkylthio, (un)substituted alkyl,

alkenyl, alkynyl, alkoxy, amino; R1R2, R2R3, R3R4, R4R5 = CH:CHCH:CH] were prepared Thus, 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine was alkylated with Me2CHI to give I-HI (R = Me2CH, R1 = R2 = Cl; R3-R5 = H) which was converted to the mesylate salt (II) (12% overall yield). II at 1 mg/kg i.v. to rats increased the amount of aconitine required to elicit ventricular arrhythmias by 490% compared with 84% for 1 mg/kg verapamil.

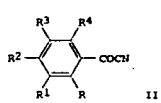
L4 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:89397 HCAPLUS
DOCUMENT NUMBER: 98:89397
TITLE: Substituted aromatic compounds
INVENTOR(S): Baxter, Martin G.; Elphick, Albert R.; Miller, Alistair A.; Sawyer, David A.
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Can., 26 pp. Division of Can. Appl. No. 353,081.
CODEN: CAXXA4
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 1133938	A2	19821019	CA 1981-373126	19810316
CA 1112643	A1	19811117	CA 1980-353081	19800530
US 4486354	A	19841204	US 1981-308805	19811005
AU 566870	B2	19871105	AU 1983-14051	19830428
US 4602017	A	19860722	US 1984-583286	19840227
FI 8400888	A	19840306	FI 1984-888	19840306
FI 73203	B	19870529		
FI 73203	C	19870910		
PRIORITY APPLN. INFO.:			GB 1979-19257 A	19790601
			CA 1980-353081 A3	19800530
			US 1980-154198 A1	19800529
			FI 1980-1758 A	19800530
			CA 1981-373126	19810316
			US 1981-302365 A1	19810915

GI



I



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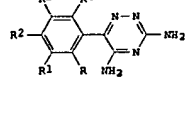


III

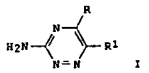
AB [(Cyanobenzylidene)amino]guanidines I (R-R4 = H, halo, alkyl, F3C; RR1 = HC:CHCH:CH, halobenzo, trifluoromethylbenzo, alkylbenzo) were prepared from the benzoyl cyanides II and H2NNHC(:NH)NH2 and were useful as intermediates in the preparation of anticonvulsant triazines III. Thus, 2,3-Cl2C6H3COCl was treated with CuCN to give 2,3-Cl2C6H3COCN which was treated with H2NNHC(:NH)NH2 to give I (R = R1 = Cl, R2 = R3 = R4 = H), which was cyclized by KOH to give III (R = R2 = Cl, R2 = R3 = R4 = H) (IV). The anticonvulsant ED50 of IV was 2.4 mg/kg in the maximal electroshock test.

L4 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:208914 HCAPLUS
DOCUMENT NUMBER: 94:208914
TITLE: 1,2,4-Triazine derivatives, pharmaceutical compositions and intermediates utilized for their preparation
INVENTOR(S): Baxter, Martin George; Elphick, Albert Reginald; Miller, Alistair Ainslie; Sawyer, David Alan
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 21121	A1	19810107	EP 1980-103032	19800530
EP 21121	B1	19830511		
R: BE, CH, DE, FR, GB, LU, NL, SE				
DK 8002338	A	19801202	DK 1980-2338	19800530
DK 153787	B	19880905		
DK 153787	C	19890116		
FI 8001758	A	19801202	FI 1980-1758	19800530
FI 67844	B	19850228		
FI 67844	C	19850610		
AU 8058906	A	19801204	AU 1980-58906	19800530
AU 530999	B2	19830804		
JP 56025169	A	19810310	JP 1980-71580	19800530
JP 01044706	B	19890929		
ES 491998	A1	19810516	ES 1980-491998	19800530
DD 151309	A5	19811014	DD 1980-221474	19800530
ZA 8003250	A	19820127	ZA 1980-3250	19800530
AT 8002896	A	19820715	AT 1980-2896	19800530
AT 370097	B	19830225		
EP 59987	A1	19820915	EP 1982-102293	19800530
EP 59987	B1	19850814		
R: BE, CH, DE, FR, GB, LU, NL, SE				
PL 124029	B1	19821231	PL 1980-224633	19800530
HU 24621	A2	19830328	HU 1980-1364	19800530
HU 182086	B	19831228		
IL 60201	A	19840531	IL 1980-60201	19800530
CS 234018	B2	19850314	CS 1980-3829	19800530
SU 1055331	A3	19831115	SU 1980-2932704	19800602
US 4486354	A	19841204	US 1981-308805	19811005
US 4602017	A	19860722	US 1984-583286	19840227
FI 8400888	A	19840306	FI 1984-888	19840306

FI 73203	B	19870529			
FI 73203	C	19870910			
JP 61033163	A	19860217	JP 1985-121370		19850604
JP 01044179	B	19890926			
PRIORITY APPLN. INFO.:			GB 1979-19257	A	19790601
			US 1980-154198	A1	19800529
			SP 1980-103032	A	19800530
			FI 1980-1758	A	19800530
			US 1981-302365	A1	19810915

OTHER SOURCE(S): MARPAT 94:208914
GI



I

AB Triazines I (R = NH2, acylamino, aminomethyleneamino; R1 = substituted Ph) were prepared Thus, 2,3-Cl2C6H3I was Grignard carboxlated and the 2,3-Cl2C6H3CO2H converted to the chloride and treated with CuCN to give 2,3-Cl2C6H3COCN which was cyclized with aminoguanidine bicarbonate to I (R = NH2, R1 = 2,3-Cl2C6H3). The latter compound had an anticonvulsant ED50 of 2.4 mg/kg orally in mice.

```
=> e US20050238724/pn,prn,an
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E2          3     US2005238723/PN
E3          1 --> US2005238724/PN
E4          0     US2005238724/PRN
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E9          1     US2005238728/PN
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E11         1     US2005238730/PN
E12         1     US2005238731/PN

=> s e3/rn
L5          0 US2005238724/RN
              (US2005238724)

=> s e3
L6          1 US2005238724/PN

=> d scan

L6    1 ANSWERS   HCAPLUS  COPYRIGHT 2007 ACS on STN
IC    ICM  A61K
CC    63-6 (Pharmaceuticals)
TI    Pharmaceutical composition containing lamotrigine particles of defined
      morphology
```



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ST    lamotrigine particle morphol seizure treatment
IT    Phenols, biological studies
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (1,6-dialkyl; pharmaceutical composition containing lamotrigine particles of
         defined morphol. and excipients)
IT    Alcohols, biological studies
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (C16-18; pharmaceutical composition containing lamotrigine particles of
defined
         morphol. and excipients)
IT    Quaternary ammonium compounds, biological studies
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (alkylbenzyldimethyl, chlorides; pharmaceutical composition containing
         lamotrigine particles of defined morphol. and excipients)
IT    Drug delivery systems
         (liqs., oral; pharmaceutical composition containing lamotrigine particles of
         defined morphol. and excipients)
IT    Drug delivery systems
         (particles; pharmaceutical composition containing lamotrigine particles of
         defined morphol. and excipients)
IT    Acacia
      Anticonvulsants
      Chondrules
      Egg yolk
      Human
      Seizures
         (pharmaceutical composition containing lamotrigine particles of defined
morphol.
         and excipients)
IT    Alcohols, biological studies
      Bentonite, biological studies
      Carbohydrates, biological studies
      Caseins, biological studies
      Gelatins, biological studies
      Kaolin, biological studies
      Polyoxyalkylenes, biological studies
      Tocopherols
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (pharmaceutical composition containing lamotrigine particles of defined
morphol.
         and excipients)
IT    Drug delivery systems
         (solids, oral; pharmaceutical composition containing lamotrigine particles
of
         defined morphol. and excipients)
IT    Fats and Glyceridic oils, biological studies
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (vegetable, hydrogenated; pharmaceutical composition containing lamotrigine
         particles of defined morphol. and excipients)
IT    Fats and Glyceridic oils, biological studies
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (vegetable; pharmaceutical composition containing lamotrigine particles of
         defined morphol. and excipients)
IT    9003-01-4D, crosslinked
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (Carbomer; pharmaceutical composition containing lamotrigine particles of
         defined morphol. and excipients)
IT    9003-39-8D, crosslinked
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
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         (Crospovidone; pharmaceutical composition containing lamotrigine particles
of
         defined morphol. and excipients)
IT    99-96-7D, alkyl esters
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (Parabens; pharmaceutical composition containing lamotrigine particles of
         defined morphol. and excipients)
IT    7631-86-9, Colloidal silicon dioxide, biological studies
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (colloidal; pharmaceutical composition containing lamotrigine particles of
         defined morphol. and excipients)
IT    9004-34-6, Cellulose, biological studies
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (microcryst.; pharmaceutical composition containing lamotrigine particles of
         defined morphol. and excipients)
IT    50-21-5, Lactic acid, biological studies   50-70-4, Sorbitol, biological
      studies   50-99-7, Dextrose, biological studies   56-81-5, Glycerin,
      biological studies   57-15-8, Chlorobutanol   57-48-7, Fructose,
      biological studies   57-50-1, Sucrose, biological studies   57-55-6,
      Propylene glycol, biological studies   57-88-5, Cholesterol, biological
      studies   60-00-4, Ethylenediamine tetraacetic acid, biological studies
      60-12-8, Phenethyl alcohol   63-42-3, Lactose   64-17-5, Ethyl alcohol,
      biological studies   64-19-7, Acetic acid, biological studies   69-65-8,
      Mannitol   72-17-3, Sodium lactate   77-92-9, Citric acid, biological
      studies   79-41-4D, Methacrylic acid, polymers   81-07-2, Saccharin
      87-69-4, biological studies   100-51-6, Benzyl alcohol, biological studies
      108-32-7, Propylene carbonate   121-54-0, Benzethonium chloride
      127-09-3, Sodium acetate   128-37-0, Butylated hydroxy toluene, biological
      studies   128-44-9, Sodium saccharin   471-34-1, Calcium carbonate,
      biological studies   526-95-4, Gluconic acid   527-07-1, Sodium gluconate
      532-32-1, Sodium benzoate   546-93-0, Magnesium carbonate   994-36-5,
      Sodium citrate   1309-48-4, Magnesium oxide, biological studies
      1327-43-1, Magnesium aluminum silicate   7447-40-7, Potassium chloride,
      biological studies   7631-90-5, Sodium bisulfite   7647-14-5, Sodium
      chloride, biological studies   7681-57-4, Sodium metabisulfite
      7758-87-4, Tribasic calcium phosphate   7778-18-9, Calcium sulfate
      7789-77-7, Dibasic calcium phosphate dihydrate   8013-17-0, Invert sugar
      8027-56-3, Liquid glucose   9000-30-0, Guar gum   9000-65-1, Tragacanth
      9000-69-5, Pectin   9002-89-5, Polyvinyl alcohol   9003-39-8, Povidone
      9004-32-4, Carboxymethylcellulose sodium   9004-53-9, Dextrin   9004-57-3,
      Ethyl cellulose   9004-62-0, Hydroxyethyl cellulose   9004-64-2,
      Hydroxypropyl cellulose   9004-65-3, Hydroxypropyl methylcellulose
      9004-67-5, Methylcellulose   9005-25-8, Starch, biological studies
      9005-32-7, Alginic acid   9005-37-2, Propylene glycol alginate
      9005-38-3, Sodium alginate   9050-04-8   9050-36-6, Maltodextrin
      9063-38-1, Sodium starch glycolate   11138-66-2, Xanthan gum   14807-96-6,
      Talc, biological studies   22839-47-0, Aspartame   25013-16-5, Butylated
      hydroxyanisole   25322-68-3, Polyethylene glycol   36653-82-4, Cetyl
      alcohol   39404-33-6, Dextrates   54182-62-6D, Polacrilin, potassium form
      74811-65-7, Croscarmellose sodium   84057-84-1, Lamotrigine
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (pharmaceutical composition containing lamotrigine particles of defined
morphol.
         and excipients)

ALL ANSWERS HAVE BEEN SCANNED

=> d his
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     (FILE 'HOME' ENTERED AT 16:55:13 ON 04 APR 2007)

     FILE 'REGISTRY' ENTERED AT 16:55:37 ON 04 APR 2007
L1             STRUCTURE UPLOADED
L2               3 S L1 SSS SAM
L3             128 S L1 SSS FULL

     FILE 'HCAPLUS' ENTERED AT 16:56:47 ON 04 APR 2007
L4              25 S LJ/P
                E US20050238724/PN,PRN,AN
L5               0 S E3/RN
L6               1 S E3

=> fil reg
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              78.55     257.16

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CA SUBSCRIBER PRICE                             -19.50     -19.50

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STRUCTURE FILE UPDATES:     3 APR 2007  HIGHEST RN 929074-02-2
DICTIONARY FILE UPDATES:    3 APR 2007  HIGHEST RN 929074-02-2

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

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predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> s 16
L7               0 US2005238724/PN

=> d his

     (FILE 'HOME' ENTERED AT 16:55:13 ON 04 APR 2007)

     FILE 'REGISTRY' ENTERED AT 16:55:37 ON 04 APR 2007
L1             STRUCTURE UPLOADED
L2               3 S L1 SSS SAM
L3             128 S L1 SSS FULL
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     FILE 'HCAPLUS' ENTERED AT 16:56:47 ON 04 APR 2007
L4             25 S L3/P
                E US20050238724/PN,PRN,AN
L5              0 S E3/RN
L6              1 S E3

     FILE 'REGISTRY' ENTERED AT 16:58:38 ON 04 APR 2007
L7              0 S L6

=> fil hcaplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                ENTRY    SESSION
FULL ESTIMATED COST                              5.85     263.01

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                ENTRY    SESSION
CA SUBSCRIBER PRICE                              0.00      -19.50

FILE 'HCAPLUS' ENTERED AT 17:00:04 ON 04 APR 2007
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FILE COVERS 1907 - 4 Apr 2007  VOL 146 ISS 15
FILE LAST UPDATED: 3 Apr 2007  (20070403/ED)

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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s lamotrigine/cn
   REGISTRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or PHITSTR) to directly view retrieved structures.



L9         1265 L8

=> s "3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine"
       6859857 "3"
       6355474 "5"
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         35536 "DIAMINO"
             3 "DIAMINOS"
         35536 "DIAMINO"
                ("DIAMINO" OR "DIAMINOS")
       3871969 "6"
       9105408 "2"
       6859857 "3"
         15829 "DICHLOROPHENYL"
      90786225 "1"
       9105408 "2"
       5555409 "4"
         41884 "TRIAZINE"
         10234 "TRIAZINES"
         44464 "TRIAZINE"
                ("TRIAZINE" OR "TRIAZINES")
L10          27 "3,5-DIAMINO-6-(2,3-DICHLOROPHENYL)-1,2,4-TRIAZINE"
                ("3"(W)"5"(W)"DIAMINO"(W)"6"(W)"2"(W)"3"(W)"DICHLOROPHENYL"(W)
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=> d scan l10 1-5
'1-5' IS NOT A VALID FORMAT FOR FILE 'HCAPLUS'

L10   27 ANSWERS   HCAPLUS  COPYRIGHT 2007 ACS on STN
IC    ICM  C07D253-06
      ICS  A61K031-53
CC    28-19 (Heterocyclic Compounds (More Than One Hetero Atom))
      Section cross-reference(s): 1, 63
TI    Preparation of 3,5-diamino-6-(
      2,3-dichlorophenyl)-1,2,
      4-triazine isethionate as an antiepileptic
ST    aminodichlorophenyltriazine isethionate prepn anticonvulsant; triazine
      diaminodichlorophenyl isethionate prepn anticonvulsant
IT    Anticonvulsants and Antiepileptics
         (diamino(dichlorophenyl)triazine.isethionate)
IT    6574-97-6, 2,3-Dichlorophenyl cyanide
      RL: RCT (Reactant); RACT (Reactant or reagent)
         (cyclocondensation of, with aminoguanidine)
IT    2582-30-1, Aminoguanidine bicarbonate
      RL: RCT (Reactant); RACT (Reactant or reagent)
         (cyclocondensation of, with dichlorophenyl cyanide)
IT    84057-84-1P
      RL: SPN (Synthetic preparation); PREP (Preparation)
         (preparation and conversion of, into isethionate salt)
IT    113170-86-8P
      RL: BAC (Biological activity or effector, except adverse); BSU (Biological
      study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
      BIOL (Biological study); PREP (Preparation); USES (Uses)
         (preparation of, as anticonvulsant)
IT    107-36-8, Isethionic acid
      RL: PROC (Process)
         (salt formation of, with diaminotriazine derivative)


The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
```



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CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
CLASS ------- IPC, NCL, ECLA, FTERM
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers;
              SCAN must be entered on the same line as the DISPLAY,
              e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, CLASS

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT)
              containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and
              its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
PHITSTR ----- First HIT RN, its text modification, its CA index name, and
              its structure diagram
PHITSEQ ----- First HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

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an arrow prompt (=>).  Examples of formats include: TI; TI,AU; BIB,ST;
TI,IND; TI,SO.  You may specify the format fields in any order and the
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specification.

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'IDE' IS NOT VALID HERE

To display more answers, enter the number of answers you would like to
see.  To end the display, enter "NONE", "N", "0", or "END".
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HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):5

L10   27 ANSWERS   HCAPLUS  COPYRIGHT 2007 ACS on STN
IC    ICM  A61K031-00
      ICS  C07D263-32
TI    Process for the preparation of 3,5-diamino-
      6-(2,3- dichlorophenyl)-1,
      2,4-triazine

L10   27 ANSWERS   HCAPLUS  COPYRIGHT 2007 ACS on STN
CC    75 (Crystallography and Liquid Crystals)
TI    Lamotrigine dimethylformamide sesquisolvate

L10   27 ANSWERS   HCAPLUS  COPYRIGHT 2007 ACS on STN
CC    25-20 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
TI    Synthesis of 2,3-Dichlorobenzonitrile
ST    dichloroaniline diazotization; dichlorophenyldiazinium prepn Sandmeyer
      reaction; dichlorobenzonitrile prepn
IT    Substitution reaction
         (Sandmeyer; preparation of dichlorobenzonitrile via diazotization of
         dichloroaniline followed by Sandmeyer reaction)
IT    608-27-5, 2,3-Dichloroaniline
      RL: RCT (Reactant); RACT (Reactant or reagent)
         (preparation of dichlorobenzonitrile via diazotization of dichloroaniline
         followed by Sandmeyer reaction)
IT    73260-77-2P
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
         (preparation of dichlorobenzonitrile via diazotization of dichloroaniline
         followed by Sandmeyer reaction)
IT    6574-97-6P, 2,3-Dichlorobenzonitrile
      RL: SPN (Synthetic preparation); PREP (Preparation)
         (preparation of dichlorobenzonitrile via diazotization of dichloroaniline
         followed by Sandmeyer reaction)

L10   27 ANSWERS   HCAPLUS  COPYRIGHT 2007 ACS on STN
IC    ICM  C07C281-18
CC    28-19 (Heterocyclic Compounds (More Than One Hetero Atom))
      Section cross-reference(s): 45
TI    Process for preparing 2-(2,3-dichlorophenyl)-2-
      (aminoguanidine)acetonitrile and a process for its cyclization into
      3,5-diamino-6-(2,3
      -dichlorophenyl)-1,2,4-
      triazine
ST    diaminodichlorophenyltriazine prepn cyclization
      dichlorophenylaminoguanidineacetonitrile
IT    Alcohols, uses
      RL: NUU (Other use, unclassified); USES (Uses)
         (aliphatic, solvents; in the cyclization of 2-(2,3-dichlorophenyl)-2-
         (aminoguanidine)acetonitrile into 3,5-
         diamino-6-(2,3-
         dichlorophenyl)-1,2,4-
         triazine)
IT    Condensation reaction catalysts
         (methanesulfonic acid; for the conversion of 2,3-dichlorobenzoyl
         cyanide with aminoguanidine bicarbonate in a non-aqueous medium to give
         2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile)
IT    Condensation reaction
         (of 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in a
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non-aqueous medium in the presence of methanesulfonic acid to give 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile)
IT Cyclization
(of 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine)
IT 75-75-2, Methanesulfonic acid
RL: CAT (Catalyst use); USES (Uses)
(condensation catalyst; in a process for preparing 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile from 2,3-dichlorobenzoyl cyanide and aminoguanidine bicarbonate)
IT 2582-30-1, Aminoguanidine bicarbonate 77668-42-9, 2,3-Dichlorobenzoyl cyanide
RL: RCT (Reactant); RACT (Reactant or reagent)
(in a process for preparing 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile)
IT 1310-73-2, Sodium hydroxide, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(in the condensation of 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in a non-aqueous medium in the presence of methanesulfonic acid to give 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile)
IT 84689-20-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparing 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile and a process for its cyclization into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine)
IT 84057-84-1P, 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for preparing 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile and a process for its cyclization into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine)
IT 64-17-5, Ethanol, uses 67-63-0, Isopropanol, uses 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; in the cyclization of 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine)

L10 27 ANSWERS HCAPLUS COPYRIGHT 2007 ACS on STN
CC 1-2 (Pharmacology)
TI Transplacental passage of lamotrigine in a human placental perfusion system in vitro and in maternal and cord blood in vivo
ST lamotrigine anticonvulsant bioavailability placenta perfusion pregnancy fetus epilepsy
IT Embryo, animal
(fetus; lamotrigine transplacental passage in human placental perfusion system in vitro and in maternal and cord blood in vivo)
IT Anticonvulsants
Drug bioavailability

Epilepsy
Human
Perfusion
Placenta
Pregnancy
(lamotrigine transplacental passage in human placental perfusion system in vitro and in maternal and cord blood in vivo)
IT Biological transport
(uptake; lamotrigine transplacental passage in human placental perfusion system in vitro and in maternal and cord blood in vivo)
IT 84057-84-1, Lamotrigine
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lamotrigine transplacental passage in human placental perfusion system in vitro and in maternal and cord blood in vivo)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> d his

(FILE 'HOME' ENTERED AT 16:55:13 ON 04 APR 2007)

FILE 'REGISTRY' ENTERED AT 16:55:37 ON 04 APR 2007
L1 STRUCTURE UPLOADED
L2 3 S L1 SSS SAM
L3 128 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 16:56:47 ON 04 APR 2007
L4 25 S L3/P
E US20050238724/PN,PRN,AN
L5 0 S E3/RN
L6 1 S E3

FILE 'REGISTRY' ENTERED AT 16:58:38 ON 04 APR 2007
L7 0 S L6

FILE 'HCAPLUS' ENTERED AT 17:00:04 ON 04 APR 2007
E LAMOTRIGINE+ALL/CT
S LAMOTRIGINE/CN

FILE 'REGISTRY' ENTERED AT 17:00:26 ON 04 APR 2007
L8 1 S LAMOTRIGINE/CN

FILE 'HCAPLUS' ENTERED AT 17:00:27 ON 04 APR 2007
L9 1265 S L8
L10 27 S 3,5-DIAMINO-6-(2,3-DICHLOROPHENYL)-1,2,4-TRIAZINE"

=> d l10 1-27 ibib abs

L10 ANSWER 1 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:365185 HCAPLUS
TITLE: Process for the preparation of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine
INVENTOR(S): Rawalnath, Sakhardande Rajiv; Kanji, Khatri Navin; Nilkanth, Firake Pandharinath; Vasant, Panchal Rajesh; Nagesh, Barekar Chandan; Madhukar, Mohite Dhanaji
PATENT ASSIGNEE(S): Saxena, Alok, India

SOURCE: Indian Pat. Appl.
CODEN: INXXBQ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 2006MU00071	A	20060421	IN 2006-MU71	20060117
PRIORITY APPLN. INFO.:			IN 2006-MU71	20060117

AB There is disclosed an improved process for the preparation of 3,5- diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine which process comprises the step of reacting 2,3-dichlorobenzoylchloride with cuprous cyanide in presence of acetonitrile without the need of a co solvent to obtain dichlorbenzoyl cyanide, said dichlorobenzoyl cyanide is reacted with amino guanidine bicarbonate to produce a schiff;s base, which is cyclized in presence of aqueous potassium hydroxide to produce 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine.

L10 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:40805 HCAPLUS
TITLE: Crystal structure of lamotriginium hydrogen phthalate dimethylformamide solvate (1:1:1)
AUTHOR(S): Sridhar, Balasubramanian; Ravikumar, Krishnan
CORPORATE SOURCE: Lab. X-ray Crystallography, Indian Inst. Chemical Technology, Hyderabad, India
SOURCE: Molecular Crystals and Liquid Crystals (2006), 461, 131-141
CODEN: MCLCD8; ISSN: 1542-1406
PUBLISHER: Taylor & Francis, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The title compound, 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine-hydrogen phthalate-dimethylformamide, $C_9H_8N_5Cl_2^+ \cdot C_8H_5O_4^- \cdot C_3H_7NO$ (lamophthalate), crystallizes in the triclinic space group P1 with unit cell parameters a = 10.1587(6) Å, b = 11.3704(7) Å, c = 12.1976(7) Å, α = 110.797(1)°, β = 111.61(1)°, γ = 99.53(1)°, V = 1151.16(12) Å3, and Z = 2. The asym. unit comprises one lamotriginium cation, one hydrogen phthalate anion, and one DMF solvate. The dihedral angle between the two planar rings is 65.3(1)°. The expected proton transfer occurs at N2 of the triazine ring. Both O-H...O and N-H...O hydrogen bonding stabilizes the crystal structure.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1032885 HCAPLUS
TITLE: Lamotrigine dimethylformamide sesquisolvate
AUTHOR(S): Sridhar, Balasubramanian; Ravikumar, Krishnan
CORPORATE SOURCE: Laboratory of X-ray Crystallography, Indian Institute of Chemical Technology, Hyderabad, 500 007, India

SOURCE: Acta Crystallographica, Section E: Structure Reports Online (2006), E62(10), o4752-o4754
CODEN: ACSEBH; ISSN: 1600-5368
URL: http://journals.iucr.org/e/issues/2006/10/00/is2071/index.html
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB In the title compound, $C_9H_7N_5Cl_2 \cdot 1.5C_3H_7NO$, the asym. unit consists of two crystallog. independent lamotrigine [systematic name: 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine] and three DMF mols. In the crystal structure, N-H···N and N-H···O hydrogen bonds lead to the formation of R22(8) and R23(8) motifs.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:421792 HCAPLUS
DOCUMENT NUMBER: 142:430313
TITLE: Process for preparation of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (Lamotrigine) via reaction of 2,3-dichlorobenzoyl chloride with cuprous cyanide and then with aminoguanidine bicarbonate followed by cyclization.
INVENTOR(S): Vyas, Sharad Kumar
PATENT ASSIGNEE(S): Torrent Pharmaceuticals Ltd., India
SOURCE: Indian, 12 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 183150	A1	19990925	IN 1998-CA2171	19981214
CA 2334937	A1	20000622	CA 1999-2334937	19991207
CA 2334937	C	20040921		
WO 2000035888	A1	20000622	WO 1999-IB1955	19991207
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000012934	A	20000703	AU 2000-12924	19991207
EP 1140872	A1	20011010	EP 1999-956293	19991207
EP 1140872	B1	20030917		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 250041	T	20031015	AT 1999-956293	19991207
RU 2231526	C2	20040627	RU 2001-115698	19991207
US 6111101	A	20000829	US 1999-456501	19991208

PRIORITY APPLN. INFO.: IN 1998-CA2171 A 19981214
WO 1999-IB1955 W 19991207
OTHER SOURCE(S): CASREACT 142:430313
AB Lamotrigine was prepared by reaction of 2,3-dichlorobenzoyl chloride with CuCN (1:1-2 molar ratio) in MeCN and a cosolvent to produce dichlorobenzoyl cyanide, reaction of the latter with aminoguanidine bicarbonate to produce the cyanoimine intermediate 2-[cyano(2,3-dichlorophenyl)methylene]hydrazinecarboximidamide, and cyclization of this in the presence of aqueous KOH at 80°-reflux.

L10 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1063399 HCAPLUS
DOCUMENT NUMBER: 143:326054
TITLE: Synthesis of 2,3-Dichlorobenzonitrile
AUTHOR(S): Deng, Hong; Liao, Qi; Zhou, Ying
CORPORATE SOURCE: Dept. of Chemistry, Central South Forestry University, Zhuzhou, Hunan Province, 412006, Peop. Rep. China
SOURCE: Jingxi Huagong Zhongjianti (2004), 34(5), 23-24
CODEN: JHZIAR; ISSN: 1009-9212
PUBLISHER: Jingxi Huagong Zhongjianti Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
OTHER SOURCE(S): CASREACT 143:326054
AB 2,3-Dichlorobenzonitrile was the important intermediate for synthesizing 2,3-dichlorobenzoic acid, which is the key intermediate for synthesizing 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine, the specific antiepileptic called Lamotrigine. 2,3-Dichlorobenzonitrile was synthesized from 2,3-dichloroaniline by diazo and Sandmeyer reaction. The yield was over 60%.

L10 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:421470 HCAPLUS
DOCUMENT NUMBER: 141:7119
TITLE: Preparation of crystalline lamotrigine and its monohydrate
INVENTOR(S): Manjunatha, Sulur G.; Kulkarni, Ashok Krishna; Kishore, Charugundia; Bokka, Ravisankar
PATENT ASSIGNEE(S): Jubilant Organosys Limited, India
SOURCE: Brit. UK Pat. Appl., 25 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2395483	A	20040526	GB 2003-15608	20030703
WO 2005003104	A2	20050113	WO 2004-IN186	20040628
WO 2005003104	A3	20050922		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: GB 2003-15608 A 20030703
OTHER SOURCE(S): CASREACT 141:7119
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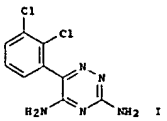


I

AB The invention relates to crystalline lamotrigine (3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine) (I) monohydrate and anhydrous lamotrigine. An improved process for manufacturing these products comprises reacting 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in aqueous mineral acid, optionally together with a water miscible organic solvent, at 30-80° to produce the 2-(2,3-dichlorophenyl)-2-(guanidinylimino)acetonitrile (Schiff base) (II). The Schiff base II is further cyclized in aqueous organic solvent, e.g. alc. to produce pure lamotrigine of a pharmaceutically acceptable quality which on further drying at 45-50° under vacuum yields lamotrigine monohydrate, and/or on further drying at 100-110° yields anhydrous lamotrigine. The lamotrigine monohydrate or anhydrous lamotrigine thereby produced may then be brought into association with a pharmaceutically acceptable carrier for administration to a patient in need thereof.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:390214 HCAPLUS
DOCUMENT NUMBER: 140:391299
TITLE: Process for preparing 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile and a process for its cyclization into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine
INVENTOR(S): Dalmases Barjoan, Pere; Bessa Bellmunt, Jordi
PATENT ASSIGNEE(S): Laboratorios Vita, S.A., Spain
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039767	A1	20040513	WO 2003-IB4763	20031027

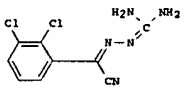
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

ES 2209639	A1	20040616	ES 2002-2502	20021031
ES 2209639	B1	20050801		
AU 2003272019	A1	20040525	AU 2003-272019	20031027
EP 1556341	A1	20050727	EP 2003-753860	20031027

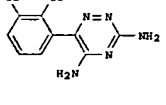
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

US 2006052625	A1	20060309	US 2005-532397	20050422
US 7179913	B2	20070220		
NO 2005002574	A	20050527	NO 2005-2574	20050527

PRIORITY APPLN. INFO.: ES 2002-2502 A 20021031
WO 2003-IB4763 W 20031027
OTHER SOURCE(S): CASREACT 140:391299
GI



I



II

AB A method for preparing the intermediate 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile (I; m.p. 180-183°) which comprises the condensation reaction of 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in a non-aqueous medium in the presence of methanesulfonic acid, which produces good I yields and short reaction times. I is cyclized into 3,5-diamino-6-(2,3

-dichlorophenyl)-1,2,4-triazine (II; m.p. 217°) under reflux in an aliph alc. (e.g., ethanol) or alc.-water mixture
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:267313 HCAPLUS
DOCUMENT NUMBER: 140:303705
TITLE: Two-step process for the synthesis of high-purity 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine from 2,3-dichlorobenzoyl cyanide and aminoguanidine dimesylate
INVENTOR(S): Neu, Jozsef; Gizur, Tibor; Toerley, Jozsef; Csabai, Janos; Vegh, Ferenc; Kalvin, Peter; Tarkanyi, Gabor
PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026845	A1	20040401	WO 2003-HU72	20030918

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

HU 200203114	A2	20040528	HU 2002-3114	20020920
CA 2498761	A1	20040401	CA 2003-2498761	20030918
AU 2003267676	A1	20040408	AU 2003-267676	20030918
EP 1539720	A1	20050615	EP 2003-748368	20030918
EP 1539720	B1	20061122		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

AT 346051	T	20061215	AT 2003-748368	20030918
IN 2005KN00267	A	20060714	IN 2005-KN267	20050224
US 2006178511	A1	20060810	US 2005-528379	20051129

PRIORITY APPLN. INFO.: HU 2002-3114 A 20020920
WO 2003-HU72 W 20030918
OTHER SOURCE(S): CASREACT 140:303705
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB High-purity 3,5-diamino-6-(

2,3-dichlorophenyl)-1,2,
4-triazine (I; i.e., lamotrigine) is prepared by the
condensation reaction of 2,3-dichlorobenzoyl cyanide (II) with 1-2 mol
equivalent of an aminoguanidine salt (e.g., aminoguanidine dimesylate) in 3-6
mol equivalent of methanesulfonic acid, then the obtained adduct (III) is
transformed without isolation into the desired product by contacting it
with magnesium oxide, followed by crystallization of the product from an
appropriate organic solvent (e.g., acetone).
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

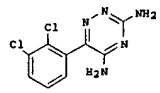
L10 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:159133 HCAPLUS
DOCUMENT NUMBER: 139:316547
TITLE: Transplacental passage of lamotrigine in a human placental perfusion system in vitro and in maternal and cord blood in vivo
AUTHOR(S): Myllynen, Paeivi K.; Pienimaeki, Paeivi K.; Vachaekangas, Kirsi H.
CORPORATE SOURCE: Department of Pharmacology and Toxicology, University of Oulu, PO Box 5000, Oulu, FIN-90014, Finland
SOURCE: European Journal of Clinical Pharmacology (2003), 58(10), 677-682
CODEN: EJCPAS; ISSN: 0031-6970
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We studied transplacental passage of lamotrigine (3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine; LTG) using an ex vivo human placental perfusion method and in in vivo samples. Term placentas from healthy mothers without medications were perfused in a recirculating dual perfusion system. LTG (2.5 μg/mL, n = 4; 10 μg/mL, n = 4) and reference compound antipyrine (100 μg/mL) were added into the maternal circulation. The disappearance of drugs from the maternal circulation and appearance into the fetal circulation was followed every 15 min up to 2 h. Drug concns. were analyzed using high-performance liquid chromatog. In addition to human placental perfusions, we analyzed LTG concns. in maternal vein and cord blood samples after delivery from two epileptic mothers receiving LTG therapy during pregnancy. LTG was detectable in the fetal circulation at 15 min in all of the perfusions, indicating rapid transfer. Maternal and fetal concns. reached equilibrium at 60 min with both concns. used. The feto-maternal ratio was 1.26 ± 0.20 with 10 μg/mL LTG and 0.83 ± 0.41 with 2.5 μg/mL LTG at the end of the perfusion. The transfer of LTG from the maternal to the fetal compartment at 120 min was 28.9 ± 10.7% with 2.5 μg/mL LTG and 37.8 ± 3.2% with 10 μg/mL LTG (p > 0.05). In the serum samples from epileptic mothers, the cord blood maternal concentration ratio was 1.02 in one pair and 1.55 in the other. LTG crossed the placenta easily and rapidly, indicating that the maternal treatment leads to a considerable fetal exposure.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:76761 HCAPLUS
DOCUMENT NUMBER: 138:137336
TITLE: Method for producing lamotrigine from alpha-oxo-2,3-dichlorophenylacetamidinoaminoguanidino

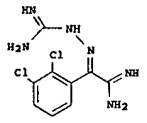
hydrazone by ring closure reaction
INVENTOR(S): Schneider, Geza; Gegoe, Csaba Lehel; Ondi, Levente; Mate, Attila Gergely; Lukacs, Ferenc; Nyerges, Miklos; Geracsi, Sandor
PATENT ASSIGNEE(S): Helm AG, Germany; CF Pharma Gyogyszergyarto Kft.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008393	A1	20030130	WO 2002-EP7433	20020704
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10134980	A1	20030213	DE 2001-10134980	20010717
DE 10134980	C2	20030528		
EP 1311492	A1	20030521	EP 2002-758308	20020704
EP 1311492	B1	20040908		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, BG, CZ, EE				
CA 2417435	C	20040113	CA 2002-2417435	20020704
CA 2417435	A1	20030130		
ES 2224074	T3	20050301	ES 2002-2758308	20020704
US 2003191310	A1	20031009	US 2003-343225	20030515
US 6683182	B2	20040127		

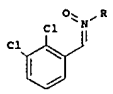
PRIORITY APPLN. INFO.: DE 2001-10134980 A 20010717
WO 2002-EP7433 W 20020704
OTHER SOURCE(S): CASREACT 138:137336; MARPAT 138:137336
GI



I



II



III

AB The invention relates to a method for producing 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine [lamotrigine (I)], or its pharmaceutically acceptable salts, by ring closure reaction from α-oxo-2,3-dichlorophenylacetamidinoaminoguanidino hydrazone (II) or its salts. The preparation of II from N-oxides, III [R = linear, branched or cyclic (un)substituted alkyl, aryl, aralkyl], or their salts, are also described. Thus, I was prepared from 2,3-Cl2C6H3CH:N(O)Ph, via cyanation with NaCN, amination to the acetamidine hydrochloride, reaction with aminoguanine bicarbonate to give II·HCl, treatment with aqueous NaOH to give the free base, which is cyclized to I; cyclization of II·HCl gives I·HCl.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:775487 HCAPLUS
DOCUMENT NUMBER: 138:60875
TITLE: Development of a solid phase extraction protocol for the simultaneous determination of anthracene and its oxidation products in surface waters by reversed-phase HPLC
AUTHOR(S): Papadoyannis, I. N.; Zotou, A.; Samanidou, V. F.
CORPORATE SOURCE: Laboratory of Analytical Chemistry, Department of Chemistry, Aristotle University of Thessaloniki, Thessaloniki, GR-541 24, Greece
SOURCE: Journal of Liquid Chromatography & Related Technologies (2002), 25(17), 2635-2653
CODEN: JLCTFC; ISSN: 1082-6076
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A gradient reversed-phase HPLC (RP-HPLC) method for the simultaneous determination

of anthracene, anthraquinone, and 1-hydroxyanthraquinone, with photodiode array detection at 250 nm, was developed. The separation was achieved on a Kromasil 100 G8 5 μm 250 × 4 mm column, applying a 10-min linear gradient elution starting with 85% methanol and 15% 0.05M ammonium acetate and ending up with 95% of methanol and 5% 0.05M ammonium acetate, at a flow-rate 0.7 mL/min, using 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (lamotrigine) as internal standard Calibration curves were rectilinear for 0.1-3.0 ng anthracene, 0.1-10.0 ng anthraquinone, and 0.5-20.0 ng 1-hydroxyanthraquinone, when 10 μL was injected. The detection limits were 0.05 ng injected on-column for anthracene and anthraquinone and 0.3 ng on-column for 1-hydroxyanthraquinone. The average intra- and inter-day RSDs for injection precision (in terms of peak area) were 1.95 and 3.62%, resp. The method was applied to the anal. of river and lake waters. A protocol, combining solid phase extraction (SPE) with sonication of matrix with sorbent, was developed for enhancement of recovery. The proposed protocol was chosen among other studied, after optimization of each step. Mean recoveries were 50% for anthracene, 71% for anthraquinone, and 105% for 1-hydroxy anthraquinone.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:435163 HCAPLUS
DOCUMENT NUMBER: 133:160143
TITLE: Evidence that DHPG-induced nociception depends on glutamate release from primary afferent C-fibres
AUTHOR(S): Lefebvre, Celeste; Fisher, Kim; Cahill, Catherine M.; Coderre, Terence J.
CORPORATE SOURCE: Pain Mechanisms Laboratory, Clinical Research Institute of Montreal, Montreal, QC, H2W 1R7, Can.
SOURCE: NeuroReport (2000), 11(8), 1631-1635
CODEN: NERPEZ; ISSN: 0959-4965
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors examined whether enhanced glutamate release contributes to the expression of persistent spontaneous nociceptive behaviors (SNBs) in rats induced by intrathecal (i.t.) administration of the selective group I mGluR agonist, (RS)-3,5-dihydroxyphenylglycine ((RS)-DHPG). Pretreatment with drugs that have been shown to inhibit glutamate release, including a group II metabotropic glutamate receptor (mGluR) agonist (2R,4R)-4-aminopyrrolidine-2,4-dicarboxylate ((2R,4R)-APDC), a group III mGluR agonist L-2-amino-4-phosphonobutyrate (L-AP4), or the use-dependent sodium channel blockers 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (lamotrigine) and 2-amino-6-trifluoromethoxybenzothiazole (riluzole), produced dose-dependent redns. in (RS)-DHPG-induced SNBs. The authors have also shown that incubation of rat lumbar spinal cord slices with (RS)-DHPG potentiates 4-aminopyridine-evoked (4-AP) release of glutamate. Furthermore, the authors found that destruction of unmyelinated primary afferent C-fibers by neonatal capsaicin treatment significantly reduced (RS)-DHPG-induced SNBs in adult rats. Together, these results suggest that (RS)-DHPG-induced nociception is dependent on spinal glutamate release, probably from primary afferent C-fibers.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:421116 HCAPLUS
DOCUMENT NUMBER: 133:60362
TITLE: An improved process for preparation of 3, 5-diamino-6-(2, 3-dichlorophenyl)-1, 2,4-triazine
INVENTOR(S): Vyas, Sharad Kumar
PATENT ASSIGNEE(S): India
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035888	A1	20000622	WO 1999-IB1955	19991207
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IN 183150	A1	19990925	IN 1998-CA2171	19981214
CA 2334937	A1	20000622	CA 1999-2334937	19991207
CA 2334937	C	20040921		
AU 2000012924	A	20000703	AU 2000-12924	19991207
EP 1140872	A1	20011010	EP 1999-956293	19991207
EP 1140872	B1	20030917		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 250041	T	20031015	AT 1999-956293	19991207
RU 2231526	C2	20040627	RU 2001-115698	19991207

PRIORITY APPLN. INFO.: IN 1998-CA2171 A 19981214
WO 1999-IB1955 W 19991207

AB 3,5-Diamino-6-(2, 3-dichlorophenyl)-1,2,4-triazine (lamotrigine) (I) useful as antiepileptic drug (no data) is prepared in a 3 step process. Thus, 2,3-dichlorobenzoylchloride was treated with cuprous cyanide in presence of acetonitrile and a solvent to produce 2,3-dichlorobenzoyl cyanide, further with aminoguanidine and cyclized to produce I.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:12098 HCAPLUS
DOCUMENT NUMBER: 132:130210
TITLE: Structure of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine isethionate solvate (lamotrigine isethionate)
AUTHOR(S): Potter, Brian; Palmer, Rex A.; Withnall, Robert;

Leach, Michael J.; Chowdhry, Babur Z.
CORPORATE SOURCE: Department of Crystallography, Birkbeck College, University of London, London, WC1E 7HX, UK
SOURCE: Journal of Chemical Crystallography (1999), 29(6), 701-706
CODEN: JCCYEV; ISSN: 1074-1542
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The crystal and mol. structure of lamotrigine isethionate was determined by direct methods. The compound crystallizes in the tetragonal space group I41/a, with a 19.684(5), c 16.557(5) Å; Z = 16, dc = 1.579; R = 0.0532, Rw = 0.1317 for 2041 reflections. Atomic coordinates are given. The isethionate moiety forms multiple H bonds to the lamotrigine nucleus, three from one isethionate, two from a symmetry related isethionate and a further two from two different symmetry related mols. Protonation of N(2') in the triazine ring, not observed in the native lamotrigine structure is presumably associated with the interaction of the isethionate moiety. Both rings in the lamotrigine moiety are essentially planar, with a dihedral angle of 66.08(7)° compared to 80.70° in native lamotrigine. The connecting bond length C(1)-C(6') 1.493(3) Å also correlates well with values in related compds. (1.480(3) Å) in the native structures.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:682978 HCAPLUS
DOCUMENT NUMBER: 132:98214
TITLE: Detection of the principal synthetic route indicative impurity in lamotrigine
AUTHOR(S): Ashton, D. S.; Ray, A. D.; Valko, K.
CORPORATE SOURCE: School of Pharmacy, University of London, London, UK
SOURCE: International Journal of Pharmaceutics (1999), 189(2), 241-248
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An anal. method has been developed for the detection of trace amts. of the principal synthetic route indicative impurity in lamotrigine (3, 5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine). A sample extract was preconcd. by normal-phase high-performance liquid chromatog. (HPLC) and analyzed by subsequent online reversed-phase HPLC-thermospray mass spectrometry (TSP-MS). During the sample extraction and concentration step, carried out by semipreparative normal-phase chromatog., the preliminary separation of the impurity from the lamotrigine takes place. The organic solvent (dichloroethane-methanol, 90:10, volume/volume) is evaporated from the collected fraction and the material is redissolved in a smaller volume of the reversed-phase mobile phase. The collected fraction is then subjected to reversed-phase HPLC-TSP-MS. The influence of an ultrasonic extraction step has been examined. When the method was applied to lamotrigine tablets, a shake flask partitioning step using 1 mg/mL EDTA in water-dichloroethane was used instead of the ultrasonic extraction. Detection limit and recovery measurements showed that the route indicative impurity formed during the synthesis could be detected in the 50-100 ppb (weight/weight)

range.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:289572 HCAPLUS
DOCUMENT NUMBER: 127:636
TITLE: A calcium antagonistic effect of the new antiepileptic drug lamotrigine
AUTHOR(S): v. Wegerer, J.; Hesslinger, B.; Berger, M.; Walden, J.
CORPORATE SOURCE: Universitaet Freiburg, Abt. Psychiatrie und Psychotherapie, Hauptstr. 5, 79104, Freiburg, Germany
SOURCE: European Neuropsychopharmacology (1997), 7(2), 77-81
CODEN: EURNE8; ISSN: 0924-977X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The new antiepileptic drug lamotrigine (LTG; 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine) has been shown to be effective in the treatment of focal epilepsies with or without secondary generalization. Furthermore, some case reports indicate an efficacy in the treatment of bipolar affective disorders. It has been suggested that the main mechanism of action of LTG is the inhibition of glutamate release through blockade of voltage sensitive sodium channels and stabilization of the neuronal membrane. Since some antidepressant drugs and the antiepileptic substance carbamazepine have calcium antagonistic properties, which may be of significance in the pathophysiol. of epilepsies and affective disorders, the interaction of lamotrigine with carbamazepine and the organic calcium channel blocker verapamil was analyzed in the low Mg2+-induced model epilepsy which has been shown to be suppressed specifically by organic calcium antagonists. Lamotrigine reduced the frequency of occurrence of low-magnesium induced field potentials in CA1 and CA3 areas of the hippocampus slice preparation (guinea pigs) in a dose-dependent manner. The subthreshold concns. which yielded no effect were 1 μmol/L for lamotrigine, 10 μmol/L for carbamazepine and 2 μmol/L for verapamil. Combinations of these subthreshold concns. elicited a reduction in the repetition rate of field potentials. The results indicate that lamotrigine behaves additive with verapamil and carbamazepine what can be due to a common action on the same subtype of calcium channels. It can be assumed that lamotrigine may have besides its action on high-frequency sodium dependent action potentials also effects on calcium channels.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:288924 HCAPLUS
DOCUMENT NUMBER: 126:312094
TITLE: Effects of lamotrigine on brain nitrite and cGMP levels during focal cerebral ischemia in rats
AUTHOR(S): Balkan, S.; Ozben, T.; Balkan, E.; Oguz, N.; Sertesen, M.; Gumuslu, S.
CORPORATE SOURCE: Department of Neurology, School of Medicine, Akdeniz University, Antalya, 07070, Turk.
SOURCE: Acta Neurologica Scandinavica (1997), 95(3), 140-146
CODEN: ANESAS; ISSN: 0001-6314
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal

LANGUAGE: English
AB Glutamate receptor antagonists are protective in animal models of focal cerebral ischemia. Lamotrigine (3,5-diamino-6-[2,3-dichlorophenyl]-1,2,4-triazine) is an anticonvulsant drug that blocks voltage-gated sodium channels and inhibits the ischemia-induced release of glutamate. Expts. in primary neuronal cultures implicate nitric oxide (NO) as a mediator of glutamatergic neurotoxicity acting via N-Methyl-D-Asparate (NMDA) receptors. The effect of glutamate release inhibitor, lamotrigine, upon NO and cGMP production has been examined in focal cerebral ischemia in rats. Focal cerebral ischemia was produced by the permanent occlusion of right middle cerebral artery (MCA) in urethane anesthetized rats. A number of indicators of brain NO production (nitrite, cGMP) were determined in ipsilateral and contralateral cerebral cortex and cerebellum after 0, 10, 60 min of focal cerebral ischemia. The same parameters were measured in rats treated with Lamotrigine (20 mg/kg, i.p.) 30 min before or just after the occlusion of the right MCA.

L10 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:546365 HCAPLUS
DOCUMENT NUMBER: 125:195693
TITLE: Preparation of lamotrigine.
INVENTOR(S): Lee, Grahame Roy
PATENT ASSIGNEE(S): Wellcome Foundation Limited, UK
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9620935	A1	19960711	WO 1995-GB3049	19951229
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9643116	A	19960724	AU 1996-43116	19951229
EP 800521	A1	19971015	EP 1995-941818	19951229
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
HU 77347	A2	19980330	HU 1997-1875	19951229
JP 11507011	T	19990622	JP 1995-520618	19951229
RU 2162081	C2	20010120	RU 1997-112921	19951229
FI 9702720	A	19970827	FI 1997-2720	19970624
US 5925755	A	19990720	US 1997-836152	19970625

PRIORITY APPLN. INFO.: GB 1994-26448 A 19941230
WO 1995-GB3049 W 19951229

AB Lamotrigine, 3,5-diamino-6-(2,3-dichlorophenyl)-5,6,2,4-triazine, is prepared by treating 6-(2,3-dichlorophenyl)-5-chloro-3-thiomethyl-1,2,4-triazine (II) with NH3. Thus, II (preparation given) was heated with ethanolic NH3 in a sealed tube at 180° and 280 psi for 72 h to give I.

L10 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:186621 HCAPLUS
DOCUMENT NUMBER: 124:278888
TITLE: Inhibition of morphine withdrawal by lamotrigine: involvement of nitric oxide
AUTHOR(S): Lizasoain, Ignacio; Leza, Juan C.; Cuellar, Beatriz; Moro, Maria A.; Lorenzo, Pedro
CORPORATE SOURCE: Departamento de Farmacologia, Facultad de Medicina, Universidad Complutense de Madrid, Avenida Complutense s/n, Madrid, 28040, Spain
SOURCE: European Journal of Pharmacology (1996), 299(1-3), 41-5
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We studied the effects of lamotrigine [3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine], a new antiepileptic compound, on naloxone-precipitated morphine withdrawal in mice. Pretreatment with lamotrigine (5-100 mg/kg, s.c.) reversed in a dose-dependent way the withdrawal-induced increase in cerebellar Ca2+-dependent nitric oxide (NO) synthase activity and reduced the number of escape jumps and other motor symptoms of abstinence, at doses that did not modify locomotor activity (25-50 mg/kg). Pretreatment with the NMDA receptor antagonist MK-801 [(+)-5-methyl-10,11-dihydroxy-5H-dibenzo[a,d]cyclohepten-5,10-imine; dizocilpine] (0.1-0.3 mg/kg, s.c.) also reversed the increase in cerebellar Ca2+-dependent NO synthase activity. However, although MK-801 reduced the number of escape jumps and other motor symptoms of abstinence, its effects were not clearly dose-dependent. Furthermore, the highest dose of MK-801 tested (0.3 mg/kg) caused an impairment of the locomotor behavior in naive mice. Thus, lamotrigine may represent a new and useful agent for the treatment of opiate abstinence.

L10 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:499316 HCAPLUS
DOCUMENT NUMBER: 123:699
TITLE: Cerebroprotective effect of lamotrigine after focal ischemia in rats
AUTHOR(S): Smith, Stuart E.; Meldrum, Brian S.
CORPORATE SOURCE: Department of Neurology, Institute of Psychiatry, Denmark Hill, SE5 8AF, UK
SOURCE: Stroke (1995), 26(1), 117-22
CODEN: SJCCA7; ISSN: 0039-2499
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Glutamate receptor antagonists are protective in animal models of focal cerebral ischemia. Lamotrigine (3,5-diamino-6-[2,3-dichlorophenyl]-1,2,4-triazine) is an anticonvulsant drug that blocks voltage-gated sodium channels and inhibits the ischemia-induced release of glutamate. The cerebroprotective effect of lamotrigine (as the isethionate salt) after middle cerebral artery occlusion was described in rats. Neurol. deficit and infarct volume (visualized by the lack of reduction of 2,3,5-triphenyltetrazolium chloride) 24 h after permanent left middle cerebral artery occlusion were studied in Fischer rats (n=8 per group per dose). Lamotrigine at 20 mg/kg i.v. over

10 min administered immediately after middle cerebral artery occlusion reduced total infarct volume by 31% and cortical infarct volume by 52%. Lamotrigine at 8 mg/kg i.v. over 10 min reduced cortical infarct volume by 38%. Lamotrigine at 50 mg/kg i.v. for 10 min was not cerebroprotective and induced a decrease of 29±15 mm Hg in mean arterial blood pressure ($P<.05$, n=8). The optimum dose of lamotrigine (20 mg/kg i.v. over 10 min) when administered with a 1-h delay after middle cerebral artery occlusion reduced cortical infarct volume by 41%. Lamotrigine (20 mg/kg i.v. over 10 min) with a 2-h delay after middle cerebral artery occlusion was ineffective. Neurol. deficits after 24 h were improved after immediate treatment with lamotrigine at 20 mg/kg i.v. over 10 min. The cerebroprotective effect of lamotrigine in rats is limited to a narrow dose range between 8 and 20 mg/kg. Lamotrigine or analogous compds. may be useful when given shortly after the onset of stroke.

L10 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:663729 HCAPLUS
DOCUMENT NUMBER: 121:263729
TITLE: Use of triazine compounds for the treatment of memory and learning disorders
INVENTOR(S): Baxter, Martin George
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9421260	A1	19940929	WO 1994-GB559	19940318
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9462176	A	19941011	AU 1994-62176	19940318
ZA 9401938	A	19950918	ZA 1994-1938	19940318
EP 689439	A1	19960103	EP 1994-909263	19940318
EP 689439	B1	20010124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08507782	T	19960820	JP 1994-520807	19940318
IL 109034	A	19981206	IL 1994-109034	19940318
AT 198831	T	20010215	AT 1994-909263	19940318
ES 2153854	T3	20010316	ES 1994-909263	19940318
PT 689439	T	20010531	PT 1994-909263	19940318
US 5866597	A	19990202	US 1997-900868	19970725
GR 3035528	T3	20010629	GR 2001-400367	20010308
PRIORITY APPLN. INFO.:			GB 1993-5693 A	19930319
			WO 1994-GB559 W	19940318
			US 1996-535140 B1	19960328

AB 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (I) and its pharmaceutically acceptable acid addition salts can be used to treat impaired memory and learning disorders. Therapeutic effects of I were demonstrated in a scopolamine-induced mouse model of memory deficit and compared with those of ondansetron HCl and piracetam. A tablet containing 150 mg I was also formulated.

L10 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:663728 HCAPLUS
DOCUMENT NUMBER: 121:263728
TITLE: Use of triazine compounds as anxiolytics
INVENTOR(S): Critchley, Martyn Alan Edwin
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9421261	A1	19940929	WO 1994-GB560	19940318
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9462177	A	19941011	AU 1994-62177	19940318
ZA 9401939	A	19950918	ZA 1994-1939	19940318
EP 689440	A1	19960103	EP 1994-909264	19940318
EP 689440	B1	20000531		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08507783	T	19960820	JP 1994-520808	19940318
JP 3633618	B2	20050330		
AT 193446	T	20000615	AT 1994-909264	19940318
ES 2147232	T3	20000901	ES 1994-909264	19940318
PT 689440	T	20001031	PT 1994-909264	19940318
US 5658905	A	19970819	US 1995-535139	19950918
GR 3033941	T3	20001130	GR 2000-401626	20000712
PRIORITY APPLN. INFO.:			GB 1993-5692 A	19930319
			WO 1994-GB560 W	19940318

AB 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (I) and its pharmaceutically acceptable acid addition salts can be used to treat anxiety and anxiety disorders. For example, an anxiolytic effect of I-isethionate was demonstrated with Vogel conflict model in rats. A tablet containing 150 mg I was also formulated.

L10 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:124865 HCAPLUS
DOCUMENT NUMBER: 120:124865
TITLE: Use of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine isethionate for the treatment and prevention of dependence on, tolerance to, and sensitization to drugs
INVENTOR(S): Nakamura-Craig, Meire
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9325207	A1	19931223	WO 1993-GB1243	19930611
W: AU, CA, CZ, GB, JP, KR, NO, NZ, PL, RU, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9343452	A	19940104	AU 1993-43452	19930611
AU 668729	B2	19960319		
EP 644763	A1	19950329	EP 1993-913346	19930611
EP 644763	B1	19970122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
GB 2282326	A	19950405	GB 1994-23697	19930611
JP 07507790	T	19950831	JP 1993-501281	19930611
AT 147980	T	19970215	AT 1993-913346	19930611
ES 2097516	T3	19970401	ES 1993-913346	19930611
CZ 284061	B6	19980812	CZ 1994-3128	19930611
IL 105986	A	19981206	IL 1993-105986	19930611
SK 279730	B6	19990211	SK 1994-1534	19930611
HR 930964	B1	20000630	HR 1993-964	19930611
JP 3439211	B2	20030825	JP 1994-501281	19930611
US 5801171	A	19980901	US 1994-347480	19941206
NO 9404790	A	19941209	NO 1994-4790	19941209
PRIORITY APPLN. INFO.:			GB 1992-12495 A	19920612
			GB 1993-8654 A	19930427
			WO 1993-GB1243 A	19930611

AB 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4,-triazine (I) and its pharmaceutically and veterinarily acceptable salts (especially the ethionate) have activity in (a) preventing or reducing dependence on, and (b) preventing or reducing tolerance or reverse tolerance to, a dependence-inducing agent such as an opioid, a central nervous system depressant, a psychostimulant, or nicotine. Thus, I (5 mg/kg orally twice a day during morphine habituation) attenuated the development of morphine tolerance in rats without affecting the analgesic effect of morphine in the tail-flick test.

L10 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:617428 HCAPLUS
DOCUMENT NUMBER: 119:217428
TITLE: Use of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine for the treatment of pain and edema
INVENTOR(S): Nakamura-Craig, Meire; Leach, Michael John
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9316700	A1	19930902	WO 1993-GB341	19930218
W: AU, CA, GB, JP, KR, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

AU 9335092	A	19930913	AU 1993-35092		19930218
AU 684711	B2	19980108			
EP 626851	A1	19941207	EP 1993-904225		19930218
EP 626851	B1	20010822			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 07503968	T	19950427	JP 1993-514628		19930218
JP 3713271	B2	20051109			
IL 104775	A	19970218	IL 1993-104775		19930218
AT 204476	T	20010915	AT 1993-904225		19930218
ES 2162813	T3	20020116	ES 1993-904225		19930218
PT 626851	T	20020228	PT 1993-904225		19930218
CA 2129043	C	20040127	CA 1993-2129043		19930218
GB 2277265	A	19941026	GB 1994-14348		19940715
GB 2277265	B	19960110			
US 5712277	A	19980127	US 1996-680111		19960715
GR 3036958	T3	20020131	GR 2001-401827		20011022
PRIORITY APPLN. INFO.:			GB 1992-3483	A	19920219
			WO 1993-GB341	A	19930218
			US 1994-284497	A1	19940804

AB The title compound (I) is useful in medicaments for the prevention or treatment of pain or edema. A tablet formulation containing I is given. I was tested in rats.

L10 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:126056 HCAPLUS
DOCUMENT NUMBER: 110:126056
TITLE: Structure of lamotrigine methanol solvate: 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine-methanol, a novel anticonvulsant drug
AUTHOR(S): Janes, Robert W.; Lisgarten, John N.; Palmer, Rex A.
CORPORATE SOURCE: Birkbeck Coll., Univ. London, London, WC1E 7HX, UK
SOURCE: Acta Crystallographica, Section C: Crystal Structure Communications (1989), C45(1), 129-32
CODEN: ACSCEE; ISSN: 0108-2701
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The title compound is monoclinic, space group P21/n, with a 15.456(3), b 11.736(2), c 7.300(3) Å, and β 94.417(3)°; Z = 4 for dc = 1.449. The final R = 0.055 for 2444 reflections. Atomic coordinates are given. The Ph and triazine aromatic rings make a dihedral angle of 80.6(9)° with each other. The bond linking the 2 rings is 1.480(3) Å. The structure is stabilized by a network of H bonds involving amino and ring N atoms, one of the Cl atoms, and the MeOH of crystallization

L10 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:112505 HCAPLUS
DOCUMENT NUMBER: 108:112505
TITLE: Preparation of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine isethionate as an antiepileptic
INVENTOR(S): Sawyer, David Alan; Copp, Frederick Charles
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 5 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 247892	A1	19871202	EP 1987-304776	19870529
EP 247892	B1	19910424		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DK 8702759	A	19871201	DK 1987-2759	19870529
DK 166278	B	19930329		
DK 166278	C	19930823		
FI 8702406	A	19871201	FI 1987-2406	19870529
FI 90770	B	19931215		
FI 90770	C	19940325		
AU 8773684	A	19871203	AU 1987-73684	19870529
AU 597982	B2	19900614		
JP 62289570	A	19871216	JP 1987-134772	19870529
JP 07051571	B	19950605		
HU 45978	A2	19880928	HU 1987-2487	19870529
HU 196769	B	19890130		
ZA 8703896	A	19890125	ZA 1987-3896	19870529
US 4847249	A	19890711	US 1987-56136	19870529
AT 62902	T	19910515	AT 1987-304776	19870529
CA 1286670	C	19910723	CA 1987-538395	19870529
IL 82710	A	19920115	IL 1987-82710	19870529
PRIORITY APPLN. INFO.:			GB 1986-13183	A 19860530
			EP 1987-304776	A 19870529

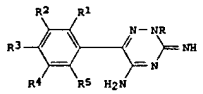
AB The title compound (I.isethionate), useful as an anticonvulsant (no data), was prepared by reaction of I with 2-hydroxyethanesulfonic acid (II) or by reaction of I salts with the anion of II. A 1.0 M solution of Na isethionate in H2O was passed through a column of IR 120 (H) ion exchange resin. I (preparation given) was added to the resulting II and the solution was filtered and evaporated Recrystn. from industrial methylated spirit gave 72% I.isethionate.

L10 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:542021 HCAPLUS
DOCUMENT NUMBER: 103:142021
TITLE: Triazine compounds having cardiovascular activity
INVENTOR(S): Allan, Geoffrey; Miller, Alastair Ainslie; Sawyer, David Alan
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 142306	A2	19850522	EP 1984-307374	19841026
EP 142306	A3	19861120		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4649139	A	19870310	US 1984-663682	19841022
DK 8405121	A	19850428	DK 1984-5121	19841026
FI 8404212	A	19850428	FI 1984-4212	19841026
AU 8434758	A	19850509	AU 1984-34758	19841026

AU 564667	B2	19870820			
JP 60109577	A	19850615	JP 1984-225636		19841026
DD 224033	A5	19850626	DD 1984-268757		19841026
HU 36102	A2	19850828	HU 1984-4003		19841026
HU 191566	B	19870330			
ES 537104	A1	19860416	ES 1984-537104		19841026
ZA 8408388	A	19860625	ZA 1984-8388		19841026
SU 1371500	A3	19880130	SU 1984-3805251		19841026
IL 73332	A	19880630	IL 1984-73332		19841026
PL 144899	B1	19880730	PL 1984-250213		19841026
CA 1261328	A1	19890926	CA 1984-466473		19841026
PRIORITY APPLN. INFO.:			GB 1983-28757	A	19831027
OTHER SOURCE(S):	MARPAT 103:142021				

GI



I

AB Tautomeric iminotriazinamines I [R = (un)substituted C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, C3-10 cycloalkyl; R1-R5 = H, halogen, alkenyloxy, acyl, acyloxy, cyano, NO2, aryl, alkylthio, (un)substituted alkyl, alkenyl, alkynyl, alkoxy, amino; R1R2, R2R3, R3R4, R4R5 = CH:CHCH:CH] were prepared Thus, 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine was alkylated with Me2CHI to give I-HI (R = Me2CH, R1 = R2 = Cl; R3-R5 = H) which was converted to the mesylate salt (II) (12% overall yield). II at 1 mg/kg i.v. to rats increased the amount of aconitine required to elicit ventricular arrhythmias by 490% compared with 84% for 1 mg/kg verapamil.

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	84.21	355.22
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-21.06	-40.56

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DICTIONARY FILE UPDATES: 3 APR 2007 HIGHEST RN 929074-02-2

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L11 1 84057-84-1/RN

=> d scan

L11 1 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
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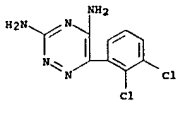
MF C9 H7 Cl2 N5
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.45	355.67
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-40.56

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FILE COVERS 1907 - 4 Apr 2007 VOL 146 ISS 15
FILE LAST UPDATED: 3 Apr 2007 (20070403/ED)

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FILE 'REGISTRY' ENTERED AT 16:55:37 ON 04 APR 2007
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L2 3 S L1 SSS SAM
L3 128 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 16:56:47 ON 04 APR 2007
L4 25 S L3/P
E US20050238724/PN,PRN,AN
L5 0 S E3/RN
L6 1 S E3

FILE 'REGISTRY' ENTERED AT 16:58:38 ON 04 APR 2007
L7 0 S L6

FILE 'HCAPLUS' ENTERED AT 17:00:04 ON 04 APR 2007
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S LAMOTRIGINE/CN

FILE 'REGISTRY' ENTERED AT 17:00:26 ON 04 APR 2007
L8 1 S LAMOTRIGINE/CN

FILE 'HCAPLUS' ENTERED AT 17:00:27 ON 04 APR 2007
L9 1265 S L8
L10 27 S "3,5-DIAMINO-6-(2,3-DICHLOROPHENYL)-1,2,4-TRIAZINE"

FILE 'REGISTRY' ENTERED AT 17:02:26 ON 04 APR 2007
L11 1 S 84057-84-1/RN

FILE 'HCAPLUS' ENTERED AT 17:02:48 ON 04 APR 2007

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L12 1265 L11

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740429 PARTICLE
814603 PARTICLES
1234571 PARTICLE
(PARTICLE OR PARTICLES)
49055 GRANULE

86594 GRANULES
111146 GRANULE
(GRANULE OR GRANULES)
L13 111187 L10 OR L12 AND PARTICLE OR GRANULE

=> s l12 near particle
MISSING OPERATOR L12 NEAR
The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

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740429 PARTICLE
814603 PARTICLES
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(PARTICLE OR PARTICLES)
L14 0 L12 (A) PARTICLE

=> s l12 (w) particle
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1234571 PARTICLE
(PARTICLE OR PARTICLES)
L15 0 L12 (W) PARTICLE

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38387 CNS
L16 46 L12 AND CNS

=> d l16 1-46 ibib abs

L16 ANSWER 1 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:259533 HCAPLUS
DOCUMENT NUMBER: 146:302318
TITLE: 5-HT1B antagonist composition for treating CNS conditions
INVENTOR(S): Harrison, Wilma Marcia; Sobolov-Jaynes, Susan Beth; Foerster, Robert Sterling, Jr.; Van Beek, Jeroen Bernard
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 46pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007026219	A2	20070308	WO 2006-IB2364	20060821
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,				

GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
JP 2007063277 A 20070315 JP 2006-233101 20060830
PRIORITY APPLN. INFO.: US 2005-712954P P 20050831
AB The present invention relates to pharmaceutical compns. comprising 5-HT1B antagonists in combination with noradrenaline re-uptake inhibitor (NRI) or serotonin noradrenaline reuptake inhibitor (SNRI) and optionally a pharmaceutically acceptable carrier, and to their medicinal use in treating or preventing CNS conditions such as depression, anxiety, cognitions, ADHD, and comorbid indications.

L16 ANSWER 2 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:226913 HCAPLUS
DOCUMENT NUMBER: 146:280994
TITLE: Reducing myocardial damage and the incidence of arrhythmia arising from loss, reduction or interruption in coronary blood flow
INVENTOR(S): Weiss, Steven Michael
PATENT ASSIGNEE(S): Australia
SOURCE: PCT Int. Appl., 47pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007022568	A1	20070301	WO 2006-AU1207	20060824
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: AU 2005-904615 A 20050825
AB A method and composition is disclosed for reducing the extent of cardiac arrhythmias, both resulting from loss, decrease or interruption to the blood supply such as may happen during a heart attack or during cardiac surgery, in mammals. In particular, the present invention relates to a method of limiting or preventing cardiac cell damage and/or death, and limiting or preventing lethal or non-lethal cardiac arrhythmias, in a human, by administering to the cardiac cells a compound which selectively blocks or partially blocks persistent sodium currents and/or persistent sodium channels of cardiac cells. The composition involves any physiol. acceptable chemical or pharmaceutical composition comprising as its active ingredient a cardiac persistent sodium current and/or persistent sodium channel blocker.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

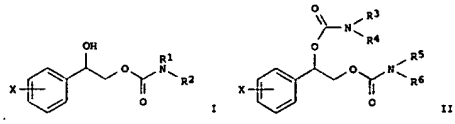
L16 ANSWER 3 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:136851 HCAPLUS

TITLE: Recent advances in anti-epileptic drugs
AUTHOR(S): Khan, S. A.; Lamba, H. S.; Rathour, Arvind; Budhwaar, Vikas; Pahwa, Rakesh; Manjusha
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Jamia Hamdard, New Delhi, 110 062, India
SOURCE: Asian Journal of Chemistry (2007), 19(2), 823-835
CODEN: AJCHEW; ISSN: 0970-7077
PUBLISHER: Asian Journal of Chemistry
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Epilepsies are a group of disorders of the CNS characterized by paroxysmal cerebral dysrhythmia, manifesting as brief episodes (seizures) of loss or disturbance of consciousness, with or without characteristic body movements (convulsions), sensory or psychiatric phenomena. Epilepsy has a focal origin in the brain, manifestations depend on the site of the focus, regions into which the discharges spread. Some newer anti-epileptic drugs have recently been developed. They have some advantages over the older drugs. These newer drugs may control seizures more effectively. They are effective in complex partial and secondary generalized seizures. These are felbamate, vigabatrin, gabapetin, clobazam, lamotrigine, oxcarbazepine, tiagabine, topiramate, fosphenytoin, and zonisamide.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:61845 HCAPLUS
DOCUMENT NUMBER: 146:135588
TITLE: Neuroprotective carbamate derivs. for treatment of neurodegenerative disorders
INVENTOR(S): Zhao, Boyu; Tywman, Roy E.
PATENT ASSIGNEE(S): Janssen Pharmaceutica, N.V., Belg.
SOURCE: PCT Int. Appl., 83pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007008562	A2	20070118	WO 2006-US26291	20060707
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2007021500	A1	20070125	US 2006-481601	20060706

PRIORITY APPLN. INFO.: US 2005-698403P P 20050712
OTHER SOURCE(S): MARPAT 146:135588
GI



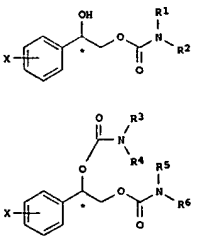
I II

AB This invention is directed to methods for providing neuroprotection comprising administering to a subject in need thereof a therapeutically effective amount of a compound selected from Formula (I) and Formula (II), where Ph is substituted at X with 1-5 halo atoms selected from F, C, B or I and R1-R6 = (un)substituted C1-C4 alkyl or pharmaceutical acceptable salts or esters thereof. Carbamate derivative decreased infarct volume following reperfusion in a rat model of transient cerebral ischemia arising from middle cerebral artery occlusion.

L16 ANSWER 5 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:61839 HCAPLUS
DOCUMENT NUMBER: 146:156257
TITLE: Carbamate compounds for treating epileptogenesis
INVENTOR(S): Twyman, Roy E.; Zhao, Boyu
PATENT ASSIGNEE(S): Janssen Pharmaceutica, N.V, Belg.
SOURCE: PCT Int. Appl., 82pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007008551	A2	20070118	WO 2006-US26277	20060707
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2007021501	A1	20070125	US 2006-481626	20060706
PRIORITY APPLN. INFO.:			US 2005-698625P	P 20050712
OTHER SOURCE(S):		MARPAT 146:156257		

GI



I II

AB The invention is directed to methods for preventing, treating, reversing, inhibiting, or arresting epileptogenesis in a subject comprising administering to the subject in need thereof a therapeutically effective amount of a compound selected from the group consisting of Formula (I) and Formula (II),, where Ph is substituted at X with F, Cl, Br, or I; and R1-R6 = (un)substituted CrC4 alkyl or a pharmaceutically acceptable salt or ester thereof. A carbamate compound demonstrated anti-epileptogenic effects in rat model of spontaneous seizures.

L16 ANSWER 6 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1207236 HCAPLUS
DOCUMENT NUMBER: 145:495703
TITLE: Methods and compositions for the treatment of CNS-related conditions
INVENTOR(S): Went, Gregory T.; Fultz, Timothy J.
PATENT ASSIGNEE(S): Neuromolecular Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 58pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006121560	A2	20061116	WO 2006-US13506	20060406
WO 2006121560	A3	20070315		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

KG, KZ, MD, RU, TJ, TM

US 2006142398	A1	20060629	US 2005-285905	20051122
PRIORITY APPLN. INFO.:			US 2005-669290P	P 20050406
			US 2005-285905	A 20051122
			US 2004-630885P	P 20041123
			US 2004-635365P	P 20041210
			US 2005-701857P	P 20050722

AB In general, the present invention provides methods and compns. for treating and preventing CNS-related conditions, such as neurodegenerative conditions (e.g., Alzheimer's disease and Parkinson's disease) and pain, by administering to a subject in need thereof a combination that includes an N-Methyl-D-Aspartate receptor (NMDAr) antagonist and a second agent such as acetylcholinesterase inhibitor (ACheI).

L16 ANSWER 7 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1173916 HCAPLUS
DOCUMENT NUMBER: 145:477933
TITLE: Methods and compositions for the treatment of CNS-related conditions
INVENTOR(S): Went, Gregory T.; Fultz, Timothy J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 29pp., Cont.-in-part of U.S. Ser. No. 285,905.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006252788	A1	20061109	US 2006-399879	20060406
US 2006142398	A1	20060629	US 2005-285905	20051122
PRIORITY APPLN. INFO.:			US 2005-669290P	P 20050406
			US 2005-285905	A2 20051122
			US 2004-630885P	P 20041123
			US 2004-635365P	P 20041210
			US 2005-701857P	P 20050722

AB The present invention provides novel methods and compns. for the treatment and prevention of CNS-related conditions. One of the CNS-related conditions treated by the methods and compns. of the invention is Alzheimer's disease.

L16 ANSWER 8 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:804735 HCAPLUS
DOCUMENT NUMBER: 146:243958
TITLE: Quantitative EEG effects of carbamazepine, oxcarbazepine, valproate, lamotrigine, and possible clinical relevance of the findings
AUTHOR(S): Clemens, Bela; Menes, Andrea; Piros, Palma; Bessenyei, Monika; Altmann, Anna; Jerney, Judit; Kollar, Katalin; Rosdy, Beata; Rozsavoelgyi, Margit; Steinecker, Katalin; Hollody, Katalin
CORPORATE SOURCE: Epilepsy Center, Department of Neurology, Kenezy Gyula Memorial Hospital, Debrecen, 4031, Hung.
SOURCE: Epilepsy Research (2006), 70(2-3), 190-199
CODEN: EPIRES; ISSN: 0920-1211
PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Quant. EEG (QEEG) effects of therapeutic doses of carbamazepine (CBZ), oxcarbazepine (OXC), valproate (VA) and lamotrigine (LA) monotherapy were investigated in patients with beginning epilepsy. Baseline waking EEG (EEG1) was recorded in the untreated state, the second EEG (EEG2) was done after 8 wk of reaching the therapeutic dose. Left occipital data were used for anal. QEEG target parameters were absolute band-power (delta: AD, theta: AT, alpha: AA, beta: AB), and alpha mean frequency (AMF). Group effects (untreated vs. treated condition in the CBZ, VA, OXC, LA groups) were computed for each target parameter. One group with benign rolandic epilepsy remained untreated for clin. reasons and served to estimate the QEEG test-retest differences. In addition, the individual QEEG response to each drug was calculated as (EEG2 - EEG1). Results: statistically significant ($p < 0.05$) group differences indicated the QEEG domain systematically affected by the drugs. CBZ caused AT increase and AMF decrease. OXC caused AMF decrease. VA and LA did not decrease AMF (LA even increased it), but reduced broad-band power. Individual power and AMF changes showed considerable variability in each group. >0.5 Hz AMF decrease (that was reported to predict cognitive impairment in prior studies) occurred in 10/41 patients in the CBZ group but never in the OXC, VA, LA groups. The results may be utilized in planning further studies addressing the relationship between antiepileptic drugs and their CNS effects. In addition, the relationship of AED-related cognitive impairment and AMF changes was discussed.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 9 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:740619 HCAPLUS
DOCUMENT NUMBER: 145:159852
TITLE: Method for treating borderline personality disorder and self-injurious behavior with glutamate-modulating agents
INVENTOR(S): Feuerstein, Seth; Coric, Vladimir
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 9 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006167068	A1	20060727	US 2006-339881	20060126
PRIORITY APPLN. INFO.:			US 2005-647535P	P 20050126

AB Glutamate-modulating agents are useful for treating borderline personality disorder and self-injurious behavior. Methods for treating borderline personality and self-injurious behavior are provided which involve administering a glutamate-modulating agent to a patient. The invention also includes combination methods of treatment in which a glutamate-modulating agent is administered with one or more other CNS active agents. Packaged pharmaceutical compns. containing a glutamate-modulating agent and one or more other CNS agent are also provided, as are packaged pharmaceutical formulations containing a glutamate-modulating agent and instructions for using the glutamate-modulating agent for treating borderline personality disorder or self-mutilating behavior.

L16 ANSWER 10 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:493860 HCAPLUS
DOCUMENT NUMBER: 144:481072
TITLE: Methods and compositions for treating pain
INVENTOR(S): Robbins, Wendye
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 61 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006111307	A1	20060525	US 2005-281771	20051116
US 2006111308	A1	20060525	US 2005-281984	20051116
WO 2006055672	A2	20060526	WO 2005-US41608	20051116
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
GB 2423928	A	20060913	GB 2006-6028	20051116
PRIORITY APPLN. INFO.:			US 2004-628646P	P 20041116
			WO 2005-US41608	W 20051116

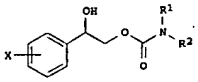
AB Methods and compns. are described for the modulation of central nervous system and/or fetal effects of substances. Methods and compns. are described for the modulation of efflux transporter activity to increase the efflux of drugs and other compds. out of a physiol. compartment and into an external environment. In particular, the methods and compns. disclosed herein provide for the increase of efflux transporter activity at blood-brain, blood-CSF and placental-maternal barriers to increase the efflux of drugs and other compds. from physiol. compartments, including central nervous system and fetal compartments.

L16 ANSWER 11 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:383992 HCAPLUS
DOCUMENT NUMBER: 144:404414
TITLE: Carbamate compounds for use in treating neurodegenerative disorders
INVENTOR(S): Twyman, Roy E.; Zhao, Boyu
PATENT ASSIGNEE(S): Janssen Pharmaceutica, N.V., Belg.
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2006044472	A1	20060427	WO 2005-US36695	20051014
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:			US 2004-619402P	P 20041015
			US 2005-698403P	P 20050712

OTHER SOURCE(S): MARPAT 144:404414
GI



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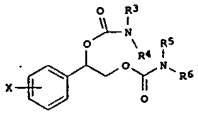

II

AB The invention discloses methods for providing neuroprotection, comprising administering to a subject in need thereof a therapeutically effective amount of a compound I or II [Ph is substituted at X with 1-5 halo atoms selected from F, Cl, Br, I; R1-R6 = H, (un)substituted C1-C4 alkyl], or a pharmaceutically acceptable salt or ester thereof.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 12 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:333530 HCAPLUS
DOCUMENT NUMBER: 144:324867
TITLE: Methods of treating epileptogenesis and epilepsy
INVENTOR(S): Choi, Yong Moon; Gordon, Robert; Novak, Gerald P.; Plata-Salaman, Carlos R.; Twyman, Roy E.; White, H. Steve; Zhao, Boyu
PATENT ASSIGNEE(S): Janssen Pharmaceutica, N.V., Belg.
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006033947	A2	20060330	WO 2005-US32861	20050915
WO 2006033947	A3	20060629		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006194873	A1	20060831	US 2005-227247	20050915
PRIORITY APPLN. INFO.:			US 2004-610276P	P 20040916
			US 2005-698625P	P 20050712
			US 2005-707242P	P 20050811

OTHER SOURCE(S): MARPAT 144:324867
AB This invention is directed to methods for preventing, treating, reversing, inhibiting or arresting epilepsy and epileptogenesis in a subject comprising administering to the subject in need thereof a therapeutically effective amount of a compound selected from the group consisting of Formula (I) and Formula (II), or a pharmaceutically acceptable salt or ester thereof,: Formula (I) Formula (II) wherein Ph is substituted at X with one to five halogen atoms selected from the group consisting of fluorine, chlorine, bromine and iodine; and, R1, R2, R3, R4, R5 and R6 are independently selected from the group consisting of hydrogen and C1-C4 alkyl; wherein C1-C4 alkyl is optionally substituted with Ph (wherein Ph is optionally substituted with substituents independently selected from the group consisting of halogen, C1-C4 alkyl, C1-C4 alkoxy, amino, nitro and cyano).

L16 ANSWER 13 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:149768 HCAPLUS
DOCUMENT NUMBER: 144:232798
TITLE: Preparation of nitroxyalkyl derivatives of phenol for treating inflammatory, cardiovascular and peripheral vascular diseases
INVENTOR(S): Ongini, Ennio; Impagnatiello, Francesco
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006015930	A1	20060216	WO 2005-EP53500	20050720
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				

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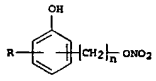
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.: US 2004-599857P P 20040810
OTHER SOURCE(S): MARPAT 144:232798
GI



I

AB The title compds. I [n = 1-20; R = H, halo, a linear or branched (C1-C10)alkoxy, OH, CF3, NHR' (wherein R' = H or a linear or branched (C1-C10)alkyl); or a salt thereof], useful for treating inflammatory disease states or disorders, cardiovascular and/or peripheral vascular diseases, were prepared E.g., a benzenemethanol, 3-hydroxy-α-nitrate (II) was prepared from com. available 3-[(hydroxy)methyl]phenol using 2-step process. Effects of II on inflammatory markers were tested. For example, the compound II applied alone or in combination with ASA inhibited LPS/INFγ-induced nitrites accumulation with similar potency as that estimated for NCX 4016 (EC50 = 58 μM and 57 μM, resp. for compound II alone and in combination with ASA). The pharmaceutical compns. comprising the compound II alone or in combination with other therapeutic agents are disclosed.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 14 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:149494 HCAPLUS
DOCUMENT NUMBER: 144:205795
TITLE: Preventing pathological increases in the rate of nerve cell suicide in immature nervous systems
INVENTOR(S): Olney, John W.
PATENT ASSIGNEE(S): Olney, John, W., USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006017524	A2	20060216	WO 2005-US27460	20050802
WO 2006017524	A3	20060831		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,				

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-598390P P 20040802

AB Methods and compds. are disclosed for reducing brain damage in fetuses, neonates, and young infants, caused by surgical anesthetics. During critical periods of synapse formation and network development in the brain, CNS neurons that do not appear to be keeping pace with certain synchronized development and connection processes are regarded as surplus, and are destroyed by a programmed cell suicide process called apoptosis. As a result, if surgical anesthetics block neuronal responses and activities that normally would indicate that a certain CNS neuron is indeed active and involved in a network and should be preserved, such anesthesia can induce apoptotic death, in the unresponsive anesthetized neurons. That process, which can cause permanent brain damage, can be minimized by manipulating certain signaling pathways that affect the balance between apoptosis-promoting proteins (e.g., Bax and Bak) and apoptosis-blocking proteins (e.g., Bcl-2 and Bcl-xL). Agents that have been tested and shown to reduce anesthesia-induced brain damage in neonatal animals include xenon (which promotes ERK MAPKinase activity), and muscarinic cholinergic agonists (which can promote ERK MAPKinase, PKA, PKC, and/or PI3K/AKT activity). Other candidate agents with similar activities include lithium, beta-1 adrenergic antagonists, and beta-2 adrenergic agonists. Such agents must intervene in the "upstream" part of the apoptosis cascade, before mitochondrial membranes become permeable and begin to release "cytochrome c" messenger mols.

L16 ANSWER 15 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:962027 HCAPLUS
DOCUMENT NUMBER: 143:235530
TITLE: Methods and compositions for the treatment of epilepsy, seizure disorders, and other CNS disorders
INVENTOR(S): Ment, Gregory; Fultz, Timothy J.; Meyerson, Lawrence
PATENT ASSIGNEE(S): Neuromolecular, Inc., USA; Neuromolecular Pharmaceuticals, Inc.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005079773	A2	20050901	WO 2005-US4819	20050214
WO 2005079773	A3	20051027		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2005215767	A1	20050901	AU 2005-215767	20050214
CA 2556214	A1	20050901	CA 2005-2556214	20050214
EP 1727538	A2	20061206	EP 2005-732251	20050214

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR

CN 1929830	A	20070314	CN 2005-80007919	20050214

PRIORITY APPLN. INFO.:

US 2004-544839P	P	20040213
US 2004-603903P	P	20040824
US 2004-635786P	P	20041213
WO 2005-US4819	W	20050214

AB The present invention relates to compns. comprising an NMDA receptor antagonists and an anti-epileptic drug for the treatment of CNS -related disorders. For example, tablets were formulated containing memantine 10, topiramate 30, dicalcium phosphate dihydrate 26.6, microcryst. cellulose 26.6, Na starch glycolate 1.2, Mg stearate 0.6, Sudragit RS30D 4.76, talc 3.3, and tri-Et citrate 0.95 mg per tablet.

L16 ANSWER 16 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:673292 HCAPLUS
DOCUMENT NUMBER: 143:172866
TITLE: Preparation of isothiazole dioxides as CXC- and CC-chemokine receptor ligands
INVENTOR(S): Taveras, Arthur G.; Zheng, Junying; Biju, Purakkattle J.; Yu, Younong; Chao, Jianhua; Fine, Jay; Lundell, Daniel; Priestley, Tony; Reggiani, Angelo; Merritt, J. Robert; Baldwin, John J.; Lai, Gaifa; Wu, Minglang
PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia Drug Discovery, Inc.
SOURCE: PCT Int. Appl., 427 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005068460	A1	20050728	WO 2004-US42720	20041220

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2550540	A1	20050728	CA 2004-2550540	20041220
US 2006025453	A1	20060202	US 2004-17505	20041220
EP 1697354	A1	20060906	EP 2004-814856	20041220

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU

CN 1918156	A	20070221	CN 2004-80041794	20041220

PRIORITY APPLN. INFO.:

US 2003-531693P	P	20031222
WO 2004-US42720	W	20041220

OTHER SOURCE(S): MARPAT 143:172866
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed are novel compds. I [D, E = N, CR50; provided that D and E are not the same (one is N and the other is CR50); R50 = H, CF3, CN, etc.; A = (hetero)aryl, (hetero)arylalkyl; B = (hetero)aryl] and the pharmaceutically acceptable salts and solvates thereof. Also disclosed is a method of treating a chemokine mediated diseases, such as, cancer, angiogenesis, angiogenic ocular diseases, pulmonary diseases, multiple sclerosis, rheumatoid arthritis, osteoarthritis, stroke and cardiac reperfusion injury, pain (e.g., acute pain, acute and chronic inflammatory pain, and neuropathic pain) using a compound I. Although the methods of preparation are not claimed, hundreds of example prepns. and/or characterization data are included. For example, II was prepared in 68% yield from the isothiazolediоxide III and the amine IV.pTSA (preparation of reactants given). Antagonist activities of some examples of I towards CXCR1, CXCR2 and CCR7 are given.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 17 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:638859 HCAPLUS
DOCUMENT NUMBER: 143:153384
TITLE: Preparation of diaminothiadiazoles as CXC- and CC-chemokine receptor ligands
INVENTOR(S): Biju, Purakkattle J.; Taveras, Arthur G.; Yu, Younong; Zheng, Junying; Chao, Jianhua; Aki, Cynthia J.; Fine, Jay; Lundell, Daniel; Priestley, Tony; Reggiani, Angelo; Merritt, J. Robert; Baldwin, John J.
PATENT ASSIGNEE(S): Schering Corporation, USA; Pharmacopeia Drug Discovery, Inc.
SOURCE: PCT Int. Appl., 593 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005066147	A1	20050721	WO 2004-US42060	20041216

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,

AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2550189	A1	20050721	CA 2004-2550189	20041216
EP 1694659	A1	20060830	EP 2004-814266	20041216

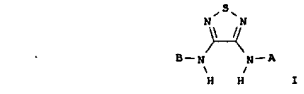
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU

US 2006223864	A1	20061005	US 2004-13753	20041216
CN 1918138	A	20070221	CN 2004-80041695	20041216

PRIORITY APPLN. INFO.:

US 2003-531311P	P	20031219
US 2003-531713P	P	20031222
WO 2004-US42060	W	20041216

OTHER SOURCE(S): MARPAT 143:153384
GI



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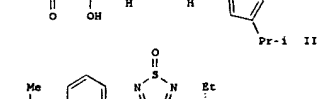
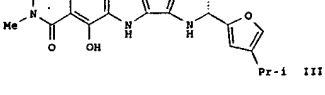


Pr-i II



Pr-i III

AB Disclosed are diaminothiadiazoles I [A = (hetero)aryl, (hetero)arylmethyl (substituted at CH2), etc.; B = (hetero)aryl] and the pharmaceutically acceptable salts and solvates thereof. Also disclosed is a method of treating a chemokine mediated diseases, such as, cancer, angiogenesis, angiogenic ocular diseases, pulmonary diseases, multiple sclerosis, rheumatoid arthritis, osteoarthritis, stroke and ischemia reperfusion injury, acute pain, acute and chronic inflammatory pain, and neuropathic pain using I. Although the methods of preparation are not claimed, hundreds of example prepns. and/or characterization data are included. For example, II was prepared in 43% yield from its monooxide III (preparation given). Antagonist activities of some examples of I towards CXCR1, CXCR2 and CCR7

are given.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 18 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:364521 HCAPLUS
DOCUMENT NUMBER: 143:126473
TITLE: Valproic acid, but not lamotrigine, suppresses seizure-induced c-fos and c-Jun mRNA expression
AUTHOR(S): Szot, Patricia; White, Sylvia S.; Shen, Danny D.; Anderson, Gail D.
CORPORATE SOURCE: Mental Illness Research Education and Clinical Center (MIRECC), VA Puget Sound Health Care System, Seattle, WA, 98108, USA
SOURCE: Molecular Brain Research (2005), 135(1-2), 285-289
CODEN: MBREE4; ISSN: 0169-328X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Seizure-induced activity was shown to increase the expression of immediate early genes (IEGs) c-fos and c-Jun in the CNS. Antiepileptic drugs (AEDs) can suppress the induction of a seizure, but it is unknown if AEDs affect the expression of seizure-induced IEGs. The authors found that valproic acid (VPA), but not lamotrigine (LTG), was capable of suppressing seizure-induced c-fos and c-Jun mRNA expression in rats despite a similar anticonvulsant effect. LTG in some regions of the CNS enhanced seizure-induced IEG expression. These studies indicate that the older AED (VPA), as compared to the newer AED (LTG), can suppress seizure-induced IEG expression. The consequence of this suppression of IEGs following a generalized seizure may be viewed either as a neuroprotective or detrimental effect upon the brain.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 19 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:288391 HCAPLUS
DOCUMENT NUMBER: 143:71550
TITLE: Adverse reactions of topiramate and lamotrigine in children
AUTHOR(S): Shechter, Tamar; Shorer, Zamir; Kramer, Uri; Lerman-Sagie, Tally; Ronen, Elisheva; Rotem, Rimona; Gorodischer, Rafael
CORPORATE SOURCE: Pharmacy Services, Soroka Medical Center, Be'er Sheva, Israel
SOURCE: Pharmacoepidemiology and Drug Safety (2005), 14(3), 187-192
CODEN: PDSAEA; ISSN: 1053-8569
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: To review the adverse drug reactions (ADRs) of Topiramate and Lamotrigine among children in Israel, and to compare the two drugs, based on their side effect profile and tolerability among this population. Methods: We performed a cross-sectional study. Four pediatric neurologists from three different tertiary medical centers in Israel documented all cases of children from birth to the age 18 years, treated with Topiramate and/or Lamotrigine in their resp. outpatient clinics and hospital wards. All present ADRs and their characteristics were recorded. Results: Reports on 45 and 65 children treated with Topiramate and

Lamotrigine resp., were received. Half of the children treated with Topiramate suffered from one or more ADRs, as opposed to one-third of the children treated with Lamotrigine (p = 0.03). Most reactions were considered mild to moderate. There were no deaths or hospitalizations, but the drug had to be discontinued in about 10% of the patients due to ADRs. Most Topiramate and Lamotrigine ADRs appeared early in the treatment and were more frequent when Topiramate was an add-on vs. a monotherapy drug. Most ADRs of both Topiramate and Lamotrigine were related to the central nervous system; while poor appetite, drowsiness, speech difficulties and weight loss were observed only with Topiramate, and rash and headaches only with Lamotrigine. Nervousness and seizure aggravation were more frequent ADRs of Topiramate whereas sleep disturbances were observed more in children treated with Lamotrigine. Conclusion: Results of this study indicate that Lamotrigine causes ADRs less frequently than Topiramate; however both medications are generally well tolerated. Topiramate and Lamotrigine differ in their central nervous system side effect profile.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 20 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:53346 HCAPLUS
DOCUMENT NUMBER: 142:290582
TITLE: Relationship between exposure and nonspecific binding of thirty-three central nervous system drugs in mice
AUTHOR(S): Maurer, Tristan S.; DeBartolo, Demetria B.; Tess, David A.; Scott, Dennis O.
CORPORATE SOURCE: Pharmacokinetics, Pharmacodynamics and Drug Metabolism, Pfizer Global Research and Development, Groton Laboratories, Groton, CT, USA
SOURCE: Drug Metabolism and Disposition (2005), 33(1), 175-181
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Unbound fractions in mouse brain and plasma were determined for 31 structurally diverse central nervous system (CNS) drugs and two active metabolites. Three comparisons were made between in vitro binding and in vivo exposure data, namely: (1) mouse brain-to-plasma exposure vs. unbound plasma-to-unbound brain fraction ratio (fuplasma/fubrain), (2) cerebrospinal fluid-to-brain exposure vs. unbound brain fraction (fubrain), and (3) cerebrospinal fluid-to-plasma exposure vs. unbound plasma fraction (fuplasma). Unbound fraction data were within 3-fold of in vivo exposure ratios for the majority of the drugs examined (i.e., 22 of 33), indicating a predominately free equilibrium across the blood-brain and blood-CSF barriers. Some degree of distributional impairment at either the blood-CSF or the blood-brain barrier was indicated for 8 of the 11 remaining drugs (i.e., carbamazepine, midazolam, phenytoin, sulpiride, thiopental, risperidone, 9-hydroxyrisperidone, and zolpidem). In several cases, the indicated distributional impairment is consistent with other independent literature reports for these drugs. Through the use of this approach, it appears that most CNS-active agents freely equilibrate across the blood-brain and blood-CSF barriers such that unbound drug concns. in brain approx. those in the plasma. However, these results also support the intuitive concept that distributional impairment does not necessarily preclude CNS activity.
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 21 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:53345 HCAPLUS
DOCUMENT NUMBER: 142:290581
TITLE: The impact of P-glycoprotein on the disposition of drugs targeted for indications of the central nervous system: Evaluation using the MDR1A/1B knockout mouse model
AUTHOR(S): Doran, Angela; Obach, R. Scott; Smith, Bill J.; Hosea, Natilie A.; Becker, Stacey; Callegari, Ernesto; Chen, Cuiping; Chen, Xi; Choo, Edna; Cianfrogna, Julie; Cox, Loretta M.; Gibbs, John P.; Gibbs, Megan A.; Hatch, Heather; Hop, Cornelis E. C. A.; Kasman, Ilana N.; LaPerle, Jennifer; Liu, JianHua; Liu, Xingrong; Logman, Michael; Maclin, Debra; Nedza, Frank M.; Nelson, Frederick; Olson, Emily; Rahematpura, Sandhya; Raunig, David; Rogers, Sabrinia; Schmidt, Kari; Spracklin, Douglas K.; Szewc, Mark; Troutman, Matthew; Tseng, Elaine; Tu, Meihua; Van Deusen, Jeffrey W.; Venkatakrishnan, Karthik; Walens, Gary; Wang, Ellen Q.; Wong, Diane; Yasgar, Adam S.; Zhang, Chenghong
CORPORATE SOURCE: Departments of Pharmacokinetics, Dynamics, and Drug Metabolism, Pfizer Global Research and Development, Groton Laboratories, Groton, CT, USA
SOURCE: Drug Metabolism and Disposition (2005), 33(1), 165-174
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thirty-two structurally diverse drugs used for the treatment of various conditions of the central nervous system (CNS), along with two active metabolites, and eight non-CNS drugs were measured in brain, plasma, and cerebrospinal fluid in the P-glycoprotein (P-gp) knockout mouse model after s.c. administration, and the data were compared with corresponding data obtained in wild-type mice. Total brain-to-plasma (B/P) ratios for the CNS agents ranged from 0.060 to 24. Of the 34 CNS-active agents, only 7 demonstrated B/P area under the plasma concentration curve ratios between P-gp knockout and wild-type mice that did not differ significantly from unity. Most of the remaining drugs demonstrated 1.1- to 2.6-fold greater B/P ratios in P-gp knockout mice vs. wild-type mice. Three, risperidone, its active metabolite 9-hydroxyrisperidone, and metoclopramide, showed marked differences in B/P ratios between knockout and wild-type mice (6.6- to 17-fold). Differences in B/P ratios and cerebrospinal fluid/plasma ratios between wild-type and knockout animals were correlated. Through the use of this model, it appears that most CNS-active agents demonstrate at least some P-gp-mediated transport that can affect brain concns. However, the impact for the majority of agents is probably minor. The example of risperidone illustrates that even good P-gp substrates can still be clin. useful CNS-active agents. However, for such agents, unbound plasma concns. may need to be greater than values projected using receptor affinity data to achieve adequate receptor occupancy for effect.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 22 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:927018 HCAPLUS

DOCUMENT NUMBER: 141:388733
TITLE: Compositions of a cyclooxygenase-2 selective inhibitor and a sodium ion channel blocker for the treatment of central nervous system damage
INVENTOR(S): Stephenson, Diane T.; Taylor, Duncan P.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004093811	A2	20041104	WO 2004-US12383	20040421
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004224940	A1	20041111	US 2004-829009	20040421
PRIORITY APPLN. INFO.:			US 2003-464499P	P 20030422
			US 2003-464830P	P 20030423

OTHER SOURCE(S): MARPAT 141:388733
AB The invention provides compns. and methods for the treatment of central nervous system damage in a subject. More particularly, the invention provides a combination therapy for the treatment of a central nervous system ischemic condition or a central nervous system traumatic injury comprising the administration to a subject of a sodium ion channel blocker in combination with a cyclooxygenase-2 selective inhibitor. Use for the treatment of stroke is specifically claimed.

L16 ANSWER 23 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:802560 HCAPLUS
DOCUMENT NUMBER: 141:301459
TITLE: Novel formulations and method of treatment
INVENTOR(S): Buxton, Ian Richard; Currie, Robin; Dela-Cruz, Myrna A.; Goodson, Gary Wayne; Karolak, Wlodzimierz; Maleki, Mehran; Iyer, Vijay Mohan; Gopal, Muppirala; Parr, Alan Frank; Sidhu, Jagdey Singh; Stagner, Robert Allen; Vijay-Kumar, Akunuri Venkata
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S. Ser. No. 629,177.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2004192690	A1	20040930	US 2003-726752		20031204
US 2005032799	A1	20050210	US 2003-629177		20030729
PRIORITY APPLN. INFO.:			GB 2002-17492	A	20020729
			GB 2002-17493	A	20020729
			GB 2003-13801	A	20030613
			US 2003-629177	A2	20030729

AB A sustained release formulation of lamotrigine or a pharmaceutically acceptable derivative thereof and methods of treatment and uses thereof are disclosed.

L16 ANSWER 24 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:740119 HCAPLUS
DOCUMENT NUMBER: 141:254587
TITLE: Methods and compositions for the treatment of chronic pain using dehydroepiandrosterone (DHEA) and derivatives thereof, alone or in combination with another drug
INVENTOR(S): Lucas, John M.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004075832	A2	20040910	WO 2004-US4861	20040219
WO 2004075832	A3	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006178354	A1	20060810	US 2005-546882	20050826
PRIORITY APPLN. INFO.:			US 2003-450271P	P 20030227
			WO 2004-US4861	W 20040219

AB The invention relates to the treatment of chronic pain using DHEA or derivs. thereof either alone or in combination with at least one other drug. The invention also includes compns. comprising DHEA or a derivative thereof and a second drug.

L16 ANSWER 25 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:120727 HCAPLUS
DOCUMENT NUMBER: 140:169680
TITLE: Sustained release formulations comprising lamotrigine
INVENTOR(S): Buxton, Ian Richard; Currie, Robin; Dela-Cruz, Myrna A.; Goodson, Gary Wayne; Karolak, Wlodzimierz; Maleki, Mehran; Iyer, Vijay Mohan; Muppirala, Gopal; Parr, Alan Frank; Sidhu, Jagdev Singh; Stagner, Robert Allen; Vijay-kumar, Akunuri Venkata
PATENT ASSIGNEE(S): Glaxo Group Limited, UK; et al.
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004012741	A1	20040212	WO 2003-EP8368	20030728
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2493301	A1	20040212	CA 2003-2493301	20030728
AU 2003260336	A1	20040223	AU 2003-260336	20030728
EP 1524981	A1	20050427	EP 2003-766343	20030728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003013148	A	20050712	BR 2003-13148	20030728
CN 1681509	A	20051012	CN 2003-822371	20030728
JP 2005536113	T	20051215	JP 2004-525362	20030728
NO 2005000948	A	20050222	NO 2005-948	20050222
PRIORITY APPLN. INFO.:			GB 2002-17492	A 20020729
			GB 2002-17493	A 20020729
			GB 2003-13801	A 20030613
			WO 2003-EP8368	W 20030728

AB A sustained-release formulation, especially tablet, of lamotrigine or its derivative
for treatment of CNS disorder comprises (by weight) 2.5 to 80% lamotrigine or its derivative, 10 to 70% release retarding polymer, 0 to 70% diluent, 0 to 20% compression aid, and 0.1 to 2.5% lubricant. Substantially all the lamotrigine or a pharmaceutically acceptable derivative is released from the formulation in a period of 2 to 20 h after administration to a patient, producing an Area Under the Curve value of 80 to 125% and Cmax of about 30% less than that of an instant-release tablet containing the same amount of lamotrigine. For example, a tablet formulation (Diffcore device) was prepared comprising (i) a core containing lamotrigine 200 mg, a blend of hydroxypropyl Me celluloses K100LV 62.64 mg and E4M 45.36 mg, lactose monohydrate 90.4 mg, and magnesium stearate 1.6 mg, and (ii) an outer coat containing Eudragit L30 D-55 (30% weight/weight solution) 17.3 mg, Red
Iron Oxide 0.37 mg, tri-Et citrate 1.81 mg, glyceryl monostearate 0.494 mg, and Polysorbate 80 0.02 mg. The coating included orifices allowing the release of lamotrigine from the core.

L16 ANSWER 26 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:61937 HCAPLUS
DOCUMENT NUMBER: 141:342
TITLE: Brain access and anticonvulsant efficacy of carbamazepine, lamotrigine, and felbamate in ABCC2/MRP2-deficient TR- rats
AUTHOR(S): Potschka, Heidrun; Fedrowitz, Maren; Loescher, Wolfgang
CORPORATE SOURCE: Department of Pharmacology, Toxicology, and Pharmacy, School of Veterinary Medicine, Hannover, Germany

SOURCE: Epilepsia (2003), 44(12), 1479-1486
CODEN: EPILAK; ISSN: 0013-9580
PUBLISHER: Blackwell Publishing, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Different ATP (ATP)driven multidrug transporters have been described to be expressed in the luminal membrane of blood-brain barrier (BBB) endothelial cells. At this site, multidrug transporters have been suggested to restrict penetration of drugs into the brain. Increasing evidence suggests that overexpression of different multidrug transporters occurs in the region of the epileptic focus of pharmacoresistant epilepsy patients. Based on the assumption that antiepileptic drugs (AEDs) are substrates of these transporters, this overexpression may limit access of AEDs to epileptic neurons and may contribute to drug-refractoriness. In a recent study, overexpression of multidrug resistance protein 2 (ABCC2; MRP2) was reported in BBB endothelial cells of epileptic focal tissue from pharmacoresistant patients. With brain microdialysis, we recently demonstrated that the AED phenytoin is subject to transport by ABCC2 at the BBB, whereas phenobarbital does not seem to be a substrate of ABCC2. We investigated whether ABCC2 is functionally involved in transport of the AEDs carbamazepine (CBZ), lamotrigine (LTG), and felbamate (FBM) across the BBB. The distribution of these AEDs into the brain of ABCC2-deficient TR- rats was determined AED concns. in plasma and brain extracellular space of these mutant rats did not differ significantly from those of rats of the corresponding background strain. In the amygdalakindling model of epilepsy, the anticonvulsant efficacy of LTG and FBM was comparable in both groups of rats. In contrast, CBZ exhibited a higher anticonvulsant activity in kindled ABCC2-deficient rats as compared with nonmutant rats. In this present study, the microdialysis results gave no evidence that ABCC2 function modulates entry of CBZ, LTG, and FBM into the CNS of naive rats. However, ABCC2 deficiency was associated with an increased anticonvulsant response of CBZ in the kindling model. Future investigations are planned to identify the underlying mechanism for this difference, clarifying whether a pharmacokinetic difference is detectable only when brain access of CBZ is compared in kindled ABCC2-deficient rats and kindled nonmutant rats, which may have an increased expression of ABCC2 in response to seizures. The data substantiate that ABCC2-deficient TR- rats are a useful tool for defining the role of ABCC2 for transport of AEDs, and give evidence that the use of kindled TR- rats may provide important supplementary information.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 27 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:962301 HCAPLUS
DOCUMENT NUMBER: 141:1649
TITLE: Glutamate-dependent regulation of cholinergic phenotype in hypothalamic neurons
AUTHOR(S): Belousov, Andrei B.
CORPORATE SOURCE: Department of Cell and Molecular Biology, Tulane University, New Orleans, LA, 70118, USA
SOURCE: NeuroReport (2003), 14(18), 2445-2449
CODEN: NERPEZ; ISSN: 0959-4965
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Glutamate NMDA receptor antagonists are used clin. However, they have serious side effects, some of which are presumably due to an increase in acetylcholine transmission. The authors' previous expts. revealed

acetylcholine-dependent excitation in rat hypothalamic cultures after a chronic glutamate receptor blockade. Dextromethorphan, amantadine, and eliprodil are NMDA receptor antagonists. Lamotrigine inhibits synaptic glutamate release. These drugs are used clin. Here, using calcium imaging and immunocytochem., the authors demonstrate that a chronic treatment with each of these drugs induced acetylcholine activity and choline acetyltransferase immunoreactivity in rat hypothalamic (but not cortical) cultures. These data support the possibility that some side effects of anti-glutamate drugs in vivo may be due to the increase in cholinergic properties in certain regions of the CNS.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 28 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:769633 HCAPLUS
DOCUMENT NUMBER: 140:263619
TITLE: Relationship between lamotrigine oral dose, serum level and its inhibitory effect on CNS: insights from transcranial magnetic stimulation
AUTHOR(S): Tergau, Frithjof; Wischer, Stephan; Somal, Hardyal S.; Nitsche, Michael A.; Mercer, A. Joe; Paulus, Walter; Steinhoff, Bernhard J.
CORPORATE SOURCE: Department of Clinical Neurophysiology, University of Gottingen, Gottingen, D-37075, Germany
SOURCE: Epilepsy Research (2003), 56(1), 67-77
CODEN: EPIRE8; ISSN: 0920-1211
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antiepileptic drug lamotrigine (LTG) is known to reduce cortical excitability evaluated by transcranial magnetic stimulation (TMS). We investigated the relationship between LTG oral dosages, serum levels and inhibitory effects on resting motor threshold (RMT), a parameter of motor system excitability assessed by TMS. In a randomized, placebo-controlled crossover study 16 male volunteers received 325 mg LTG as a single dose, as bi-hourly graded cumulative dose, or placebo. RMT and serum levels were measured before and after 2-8 h. With single dose, RMT elevation showed a poor but significant correlation to serum levels. With graded dose, serum levels as well as RMT increased dose-dependently with significant ($P<0.0001$) linear correlation. However, detailed comparison showed a high inter-individual variability in the relationship resembling a sigmoid correlation. Different mechanisms besides the sodium-channel blockage as the main mode of action of LTG are discussed to explain the diversity of individual dose-response relationships. Provided that the RMT elevation reflects the antiepileptic potential of LTG, TMS may be developed as a tool to monitor interindividual response of epilepsy patients to LTG treatment as well as to explore efficacy of other antiepileptic drugs with similar mode of action.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 29 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:376842 HCAPLUS
DOCUMENT NUMBER: 138:385297
TITLE: Methods for treating depression and other CNS disorders using enantiomerically enriched desmethyl- and didesmethyl- metabolites of citalopram
INVENTOR(S): Bush, Larry R.; Currie, Mark G.; Senanayake, Chris H.; Fang, Kevin Q.

PATENT ASSIGNEE(S): Sepracor, Inc., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040121	A1	20030515	WO 2002-US35408	20021105
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2465186	A1	20030515	CA 2002-2465186	20021105
AU 2002356903	A2	20030519	AU 2002-356903	20021105
EP 1446396	A1	20040818	EP 2002-802848	20021105
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002013949	A	20040831	BR 2002-13949	20021105
HU 2004001934	A2	20050128	HU 2004-1934	20021105
JP 2005510518	T	20050421	JP 2003-542167	20021105
CN 1705654	A	20051207	CN 2002-822084	20021105
IN 2004KN00505	A	20060616	IN 2004-KN505	20040419
ZA 2004003409	A	20051026	ZA 2004-3409	20040505
US 2004266864	A1	20041230	US 2004-842055	20040507
NO 2004002013	A	20040514	NO 2004-2013	20040514

PRIORITY APPLN. INFO.: US 2001-337608P P 20011108
WO 2002-US35408 W 20021105

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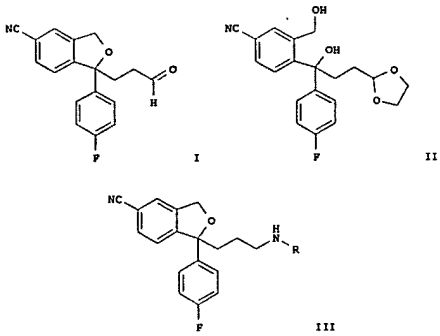


I II III

AB This invention relates to the preparation of I and II and derivs. of I and II in their racemic, enantiomerically enriched, or optically pure forms. This invention further relates to novel compns. of matter containing enantiomerically enriched (-)-desmethylcitalopram (-)-III (R = Me), (+)-didesmethylcitalopram (+)-III (R = Me), or (-)-didesmethylcitalopram (-)-III (R = H) or mixts. thereof in optimal ratios. Contrary to prior teachings, the enantiomerically enriched citalopram metabolites disclosed herein possess potent serotonin reuptake inhibitory activity, with minimal inhibitory effects on the reuptake of other known monoamines, e.g., norepinephrine (NE) or dopamine (DA). For example, stepwise reaction of 1-oxo-1,3-dihydroisobenzofuran-5-carbonitrile with 4-fluorophenylmagnesium bromide and the chiral Grignard reagent, which was prepared from 2-(2-bromoethyl)-[1,3]dioxolane and Mg powder, in THF gave II. Cyclization using mesyl chloride in CH2Cl2, followed by reduction provided the I. Reaction of the aldehyde with (-)-tert-butylsulfinamide in the presence of Ti(OEt)4 in EtOH afforded the sulfinamide, which was reduced to the amine III (R = H) with 10% HCl in MeOH. Protection of the amine with BOC anhydride in the presence of TEA in CH2Cl2 provided the enantiomerically enriched isomers, which were separated on a chiral column and subsequently deprotected with TFA to give (+)-III (R = H) and (-)-III (R = H). In biol. assays, (-)-III (R = H) and (+)-III (R = H) strongly inhibited serotonergic 5-HT receptor activity with Ki values of 5.8 nM and 90 nM, resp., with little effect on NE and DA transporter activity. By comparison, racemic citalopram inhibited serotonin reuptake with a Ki of 3.9 nM. The present invention also discloses methods for treating disorders, dysfunctions and diseases for which inhibition of serotonin reuptake is therapeutically beneficial. In particular, the present invention discloses a method for treating various forms of depression and other CNS disorders with pharmaceutical compns. described herein.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 30 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:319348 HCAPLUS
DOCUMENT NUMBER: 138:331688
TITLE: Methods of suppressing microglial activation and systemic inflammatory responses
INVENTOR(S): Laskowitz, Daniel T.; Matthew, William D.; McMillian, Michael
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 48 pp., Cont.-in-part of U.S. Ser. No. 957,909.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003077641	A1	20030424	US 2002-252120	20020923
US 2002164789	A1	20021107	US 2001-957909	20010921

PRIORITY APPLN. INFO.: US 1998-77551P P 19980311
US 1999-260430 B2 19990301
US 2001-957909 A2 20010921

AB Methods of suppressing the activation of microglial cells in the Central Nervous System (CNS), methods of ameliorating or treating the neurol. effects of cerebral ischemia or cerebral inflammation, and methods of combating specific diseases that affect the CNS by administering a compound that binds to microglial receptors and prevents or reduces microglial activation are described. ApoE receptor binding peptides that may be used in the methods of the invention are also described, as are methods of using such peptides to treat peripheral inflammatory conditions such as sepsis. Also described are methods of screening compds. for the ability to suppress or reduce microglial activation. Injection of ApoE (133-149) in mice suppressed serum levels of TNFα and IL-6 following LPS administration.

L16 ANSWER 31 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:854041 HCAPLUS
DOCUMENT NUMBER: 139:111447
TITLE: Therapeutic Drug Monitoring of Lamotrigine in Patients Suffering from Resistant Partial Seizures
AUTHOR(S): Benetello, Pierpaola; Furlanut, Marco; Baraldo, Massimo; Tonon, Agnese; Furlanut, Mario
CORPORATE SOURCE: Department of Neurological Sciences, University of Padua, Padua, Italy
SOURCE: European Neurology (2002), 48(4), 200-203
CODEN: EUNEAP; ISSN: 0014-3022
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sixty patients, all potential candidates for ongoing lamotrigine (LTG) treatment as add-on therapy for resistant partial seizures and receiving carbamazepine (CBZ) and/or valproate (VPA) treatment, were submitted to therapeutic drug monitoring (TDM). The aim was to evaluate the possible relation between serum levels and the clin. effect of LTG, to verify whether CNS toxicity has to be considered the result of a pharmacokinetic or a pharmacodynamic interaction with CBZ, and to

investigate whether possible changes in the clin. response during long-term treatment are dependent on LTG serum level variations. Sixteen patients achieved complete control, 26 a ≥50% reduction in seizures, the remainder did not respond. Mean LTG serum concns. were higher in responders than in nonresponders, the difference being statistically insignificant. The best results were observed in VPA-cotreated patients with the highest LTG blood levels. CNS toxicity occurred after giving LTG to subjects who subsequently developed the highest LTG concns., whereas CNS toxicity seemed unrelated to CBZ and CBZ-epoxide serum concns. No decrease in LTG, CBZ and VPA serum levels was observed even in patients showing a reduction in the response during long-term treatment.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 32 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:797249 HCAPLUS
DOCUMENT NUMBER: 139:29927
TITLE: Anticonvulsants in central pain
AUTHOR(S): Finnerup, Nanna B.; Gottrup, Hanne; Jensen, Troels S.
CORPORATE SOURCE: Department of Neurology and Danish Pain Research Centre, Aarhus University Hospital, Aarhus, 8000, Den.
SOURCE: Expert Opinion on Pharmacotherapy (2002), 3(10), 1411-1420
CODEN: EOPHF7; ISSN: 1465-6566
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Treatment of central neuropathic pain (CP) following lesions of the CNS is a great challenge to the clinician. Preclin. and clin. studies indicate that neuronal hyperexcitability in damaged areas of the central nervous system plays a major role in the development of CP. Anticonvulsants are thought to act by increasing γ-aminobutyric acid-mediated inhibition, decreasing abnormal neuronal hyperexcitability by modulating sodium and calcium channels or by inhibiting excitatory amino acid actions. The resulting inhibition of excess neuronal activity is thought to be the basis for the use of anticonvulsants in epilepsy as well as neuropathic pain. Both first-generation anticonvulsant drugs (e.g., phenytoin, benzodiazepines, valproate and carbamazepine) and second-generation anticonvulsant drugs (e.g., lamotrigine, gabapentin and topiramate) are used in CP conditions. However, few randomized controlled trials on the treatment of this condition have been published. Present suggestions for anticonvulsant treatment of CP are lamotrigine as the first choice, followed by gabapentin or carbamazepine/oxcarbazepine. These compds. are considered as effective as the antidepressant amitriptyline.
REFERENCE COUNT: 106 THERE ARE 106 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 33 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:672895 HCAPLUS
DOCUMENT NUMBER: 138:297430
TITLE: Lamotrigine derivatives and riluzole inhibit INa,P in cortical neurons
AUTHOR(S): Spadoni, Francesca; Hainsworth, Atticus Henry; Mercuri, Nicola Biagio; Caputi, Luigi; Martella, Giuseppina; Lavaroni, Franco; Bernardi, Giorgio; Stefani, Alessandro
CORPORATE SOURCE: IRCCS Fondazione Santa Lucia, Rome, Italy

SOURCE: NeuroReport (2002), 13(9), 1167-1170
CODEN: NERPEZ; ISSN: 0959-4965
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The persistent, slowly inactivating fraction of the sodium current (INa,P) is involved in key functions in the CNS such as dendritic integration of synaptic inputs and cellular excitability. We have studied whether established anti-epileptic drugs and neuroprotective agents target the persistent sodium current. Two lamotrigine derivs. (sipatrigine and 202W92) and riluzole inhibited the persistent sodium current at low, therapeutic concns. In contrast, lamotrigine and the classical antiepileptic agents phenytoin and valproic acid blocked the fast-inactivating sodium channel but failed to affect the persistent fraction. The ability to influence either mode of channel activity may represent a defining feature of each drug subclass, changing profoundly their clin. indications. Given the damaging role of a sustained influx of sodium in both pharmaco-resistant seizures or excitotoxic insults, we suggest the utilization of drugs that suppress the persistent conductance.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 34 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:488246 HCAPLUS
DOCUMENT NUMBER: 137:57576
TITLE: Methods and compositions using ion-dependent cotransporter modulators for treating conditions of the central and peripheral nervous systems using non-synaptic mechanisms
INVENTOR(S): Hochman, Daryl W.
PATENT ASSIGNEE(S): Cytoscan Sciences L.L.C., USA
SOURCE: U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S. Ser. No. 470,637.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002082252	A1	20020627	US 2002-56528		20020123
US 6495601	B1	20021217	US 1999-470637		19991222
US 2005267103	A1	20051201	US 2005-101000		20050407
US 2006025387	A1	20060202	US 2005-130945		20050517
US 2006089350	A1	20060427	US 2005-251724		20051017
US 2006035914	A1	20060216	US 2005-259532		20051025
			US 1998-113620P	P	19981223
			US 1999-470637	A2	19991222
			US 2001-263830P	P	20010123
			US 2002-56528	A2	20020123
			US 2005-101000	A2	20050407
			US 2005-130945	A2	20050517

PRIORITY APPLN. INFO.:

AB The invention discloses methods and compns. for treating selected conditions of the central and peripheral nervous systems employing non-synaptic mechanisms. More specifically, one aspect of the invention provides methods and materials for treating seizure and seizure disorders, epilepsy, status epilepticus, migraine, spreading depression, intracranial hypertension; for treating the pathophysiol. effects of head trauma,

stroke, ischemia and hypoxia; for treating or protecting from the pathophysiol. effects of neurotoxic agents such as ethanol; and for treating neurophsyciatric disorders and central nervous system edema by administering agents that modulate ionic concns. and/or ionic gradients in the brain, particularly ion-dependent or cation-chloride cotransporter antagonists. Electrolyte cotransport antagonists and combinations of such compns. with other agents for treating various conditions are disclosed. The invention also discloses methods and compns. for treating pain by administering ion-dependent cotransporter antagonists. Methods and compns. for enhancing cortical function, e.g. in centers of cognition, learning, and memory, by administering ion-dependent cotransporter agonists are disclosed.

L16 ANSWER 35 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:375796 HCAPLUS
DOCUMENT NUMBER: 137:5563
TITLE: Diet enriched with omega-3 fatty acids alleviates convulsion symptoms in epilepsy patients
AUTHOR(S): Schlanger, Simon; Shinitzky, Meir; Yam, Daniel
CORPORATE SOURCE: The Kalanit Institute for the Retarded Child, Rishon LeZion, Israel
SOURCE: Epilepsia (2002), 43(1), 103-104
CODEN: EPILAK; ISSN: 0013-9580
PUBLISHER: Blackwell Publishing, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We examined whether a dietary supplement containing omega-3 polyunsatd. fatty acids (n-3 PUFAs) can alleviate and/or reduce the frequency of epileptic seizures in patients with central nervous system (CNS) diseases treated with anticonvulsive drugs (ACDs). A special spread containing 65% n-3 PUFAs was added to the daily diet. The patients consumed 5 g of this spread at every breakfast for 6 mo. Five patients completed the study. In all of them, a marked reduction in both frequency and strength of the epileptic seizures was recorded. Incorporation of the dietary supplement containing n-3 PUFAs may be beneficial in suppression of some cases of epileptic seizures.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 36 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:195041 HCAPLUS
DOCUMENT NUMBER: 137:91443
TITLE: GABA and glutamate in migraine
AUTHOR(S): D'Andrea, Giovanni; Granella, Franco; Cataldini, Morena; Verdelli, Flavio; Balbi, Tiziana
CORPORATE SOURCE: Headache and Related Disorders Center, Pathology Unit, Este-Monselice Hospital, Este-Monselice, Italy
SOURCE: Journal of Headache and Pain (2001), 2(Suppl. 1), S57-S60
CODEN: JHPOAT; ISSN: 1129-2369
PUBLISHER: Springer-Verlag Italia Srl
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. GABA and glutamic acid are the main inhibitory and excitatory neurotransmitters of central nervous system. Among other functions they modulate the pain threshold in the CNS. For this reason it has been hypothesized that anomalies of GABA and glutamate turn-over may play a role in migraine pathogenesis. In this review are discussed the evidences in favor of this hypothesis. A derangement of GABA may be an

important factor in the occurrence of migraine attacks and their recurrence, whereas high level of glutamic acid may represent a biochem. marker of the neuronal hyperexcitability that may be the underlying cause of the aura. The pharmacol. modulation of metabolism of both neurotransmitters is a promising approach to improve migraine therapy. In particular the studies presented here suggest that gabaergic drugs may be useful in migraine without aura, antiglutamatergic drugs are indicated to treat migraine with aura.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 37 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:10280 HCAPLUS
DOCUMENT NUMBER: 136:64150
TITLE: GABA-ergic agonists for the treatment of age-related brain cortical dysfunction
INVENTOR(S): Leventhal, Audie G.
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000221	A1	20020103	WO 2001-US19719	20010620
W: AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2413405	A1	20020103	CA 2001-2413405	20010620
AU 2001068609	A5	20020108	AU 2001-68609	20010620
EP 1303280	A1	20030423	EP 2001-946582	20010620
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004023952	A1	20040205	US 2002-311821	20021217
AU 2006203432	A1	20060831	AU 2006-203432	20060809
			US 2000-213388P	P 20000623
			US 2001-277427P	P 20010320
			WO 2001-US19719	W 20010620

PRIORITY APPLN. INFO.:

AB Methods are disclosed for the improvement of age-related decreases in cortical function by increasing the activity of inhibitory pathways, such as GABA-ergic pathways, in the central nervous system. In particular examples, subjects with age-related decreases in cortical function are treated by administration of therapeutically effective amts. of a GABA-ergic agonist. The disclosed methods also enable screening for drugs that inhibit an age-related decline in cortical function, for example by exposing a subject to a test agent, and measuring an increase in GABA-ergic cortical inhibitory activity.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 38 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:904923 HCAPLUS
DOCUMENT NUMBER: 136:181219
TITLE: Effect of lamotrigine on the Ca2+-sensing cation current in cultured hippocampal neurons
AUTHOR(S): Xiong, Zhi-Gang; Chu, Xiang-Ping; MacDonald, J. F.
CORPORATE SOURCE: Robert S. Dow Neurobiology Laboratories, Legacy Clinical Research and Technology Center, Portland, OR, 97232, USA
SOURCE: Journal of Neurophysiology (2001), 86(5), 2520-2526
CODEN: JONEA4; ISSN: 0022-3077
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

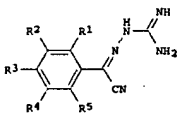
AB Concns. of extracellular calcium ([Ca2+]e) in the CNS decrease substantially during seizure activity. The authors have demonstrated previously that decreases in [Ca2+]e activate a novel calcium-sensing nonselective cation (csNSC) channel in hippocampal neurons. Activation of csNSC channels is responsible for a sustained membrane depolarization and increased neuronal excitability. This study has suggested that the csNSC channel is likely involved in generating and maintaining seizure activities. In the present study, the effects of anti-epileptic agent lamotrigine (LTG) on csNSC channels were studied in cultured mouse hippocampal neurons using patch-clamp techniques. At a holding potential of -60 mV, a slow inward current through csNSC channels was activated by a step reduction of [Ca2+]e from 1.5 to 0.2 mM. LTG decreased the amplitude of csNSC currents dose dependently with an IC50 of 171 ± 25.8 (SE) μM. The effect of LTG was independent of membrane potential. In the presence of 300 μM LTG, the amplitude of csNSC current was decreased by 31 ± 3% at -60 mV and 29 ± 2.9% at +40 mV ($P > 0.05$). LTG depressed csNSC current without affecting the potency of $Ca2+$ block of the current (IC50 for $Ca2+$ block of csNSC currents in the absence of LTG: 145 ± 18 μM; in the presence of 300 μM LTG: 136 ± 10 μM. $n = 5$, $P > 0.05$). In current-clamp recordings, activation of csNSC channel by reducing the [Ca2+]e caused a sustained membrane depolarization and an increase in the frequency of spontaneous firing of action potentials. LTG (300 μM) significantly inhibited csNSC channel-mediated membrane depolarization and the excitation of neurons. Fura-2 ratiometric $Ca2+$ imaging experiment showed that LTG also inhibited the increase in intracellular $Ca2+$ concentration induced by csNSC channel activation. The effect of LTG on csNSC channels may partially contribute to its broad spectrum of anti-epileptic actions.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 39 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:631908 HCAPLUS
DOCUMENT NUMBER: 135:195578
TITLE: Process for preparing substituted benzoyl cyanide amidinohydrazones as intermediates for synthesis of 3,5-diamino-6-phenyl-1,2,4-triazines
INVENTOR(S): Nadaka, Vladimir; Lexner, Jael; Kaspi, Joseph
PATENT ASSIGNEE(S): Chemagis Ltd., Israel
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1127873	A2	20010829	EP 2001-103660	20010223
EP 1127873	A3	20030507		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
IL 134730	A	20031031	IL 2000-134730	20000225
CA 2337280	A1	20010825	CA 2001-2337280	20010215
HU 200100740	A2	20011128	HU 2001-740	20010215
US 2001025118	A1	20010927	US 2001-789634	20010222
US 6329521	B2	20011211		

PRIORITY APPLN. INFO.: IL 2000-134730 A 20000225
OTHER SOURCE(S): CASREACT 135:195578; MARPAT 135:195578
GI



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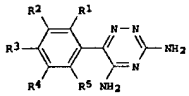

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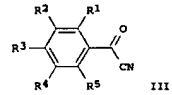


III

AB The title compds. [I; R1-R5 = H, halo, alkyl, etc.], useful as intermediates for synthesis of 1,2,4-triazines II (active in the treatment of CNS disorders), were prepared by reacting the benzoyl cyanides III with aminoguanidine bicarbonate in a mixture of a water-soluble solvent and polyphosphoric acid. Thus, reacting 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in the presence of polyphosphoric acid in MeCN afforded 2,3-dichlorobenzoyl cyanide amidinohydrazone which was then heated under reflux in PrOH to give 2,3-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine.

L16 ANSWER 40 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:237425 HCAPLUS
DOCUMENT NUMBER: 130:291518
TITLE: Analysis of CSF amino acids in young patients with generalized refractory epilepsy during an add-on study with lamotrigine
AUTHOR(S): Eriksson, Ann-Sofie; O'Connor, William T.
CORPORATE SOURCE: Department of Pediatrics, Karolinska Hospital,

Stockholm, Swed.
SOURCE: Epilepsy Research (1999), 34(1), 75-83
CODEN: EPIRE8; ISSN: 0920-1211
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of add-on administration of lamotrigine (1-12 mg/kg per day, 2-12 mo) on the levels of neurotransmission related amino acids including γ-aminobutyric acid (GABA), glutamate, aspartate, glycine and antiepileptic drugs (AEDs) in lumbar cerebrospinal fluid (CSF) was studied in 22 children and young adults with generalized therapy resistant epilepsy. Two lumbar punctures were performed, one prior to, and one following a mean of 5 mo (2-12 mo) of lamotrigine treatment. Lamotrigine decreased seizure incidence and severity in 12 of the 22 patients without influencing CSF GABA, glutamate, aspartate or glycine levels. Lamotrigine did not alter the concns. of AEDs in CSF or plasma. However, CSF GABA levels were 86% higher in those patients also treated with γ-vinyl-GABA (vigabatrin, GVG) compared with patients treated with other combinations and this was not altered by co-medication with lamotrigine. The proposed mechanism of action of lamotrigine, namely that it may inhibit glutamate release in the CNS, is not reflected by changes in CSF glutamate levels. The present findings indicate that CSF GABA, glutamate, aspartate and glycine levels may not be useful as in vivo neurochem. markers in young patients responding to the therapeutic dose of lamotrigine used in this study.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 41 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:567031 HCAPLUS
DOCUMENT NUMBER: 129:270545
TITLE: Mechanisms of deafferentation-induced plasticity in human motor cortex
AUTHOR(S): Ziemann, Ulf; Hallett, Mark; Cohen, Leonardo G.
CORPORATE SOURCE: Human Cortical Physiology Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, 20892-1428, USA
SOURCE: Journal of Neuroscience (1998), 18(17), 7000-7007
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Deafferentation induces rapid plastic changes in the cerebral cortex, probably via unmasking of pre-existent connections. Several mechanisms may contribute, such as changes in neuronal membrane excitability, removal of local inhibition, or various forms of short- or long-term synaptic plasticity. To understand further the mechanisms involved in cortical plasticity, we tested the effects of CNS-active drugs in a plasticity model, in which forearm ischemic nerve block (INB) was combined with low-frequency repetitive transcranial magnetic stimulation (rTMS) of the deafferented human motor cortex. RTMS was used to upregulate the plastic changes caused by INB. We studied six healthy subjects. In two control sessions without drug application, INB plus rTMS increased the motor-evoked potential (MEP) size and decreased intracortical inhibition (ICI) measured with single- and paired-pulse TMS in the biceps brachii muscle proximal to INB. A single oral dose of the benzodiazepine lorazepam (2 mg) or the voltage-gated Na+ and Ca2+ channel blocker lamotrigine (300 mg) abolished these changes. The NMDA receptor blocker dextromethorphan (150 mg) suppressed the reduction in ICI but not the increase

in MEP size. With sleep deprivation, used to eliminate sedation as a major factor of these drug effects, INB plus rTMS induced changes similar to that seen in the control sessions. The findings suggest that (1) the INB plus rTMS-induced increase in MEP size involves rapid removal of GABA-related cortical inhibition and short-term changes in synaptic efficacy dependent on Na+ or Ca2+ channels and that (2) the long-lasting (>60 min) reduction in ICI is related to long-term potentiation-like mechanisms given its duration and the involvement of NMDA receptor activation.
REFERENCE COUNT: 85 THERE ARE 85 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 42 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:105002 HCAPLUS
DOCUMENT NUMBER: 128:213312
TITLE: Carbamazepine toxicity with lamotrigine: pharmacokinetic or pharmacodynamic interaction?
AUTHOR(S): Besag, F. M. C.; Berry, D. J.; Pool, F.; Newbery, J. E.; Subel, B.
CORPORATE SOURCE: St Piers Lingfield, Surrey, RH7 6PW, UK
SOURCE: Epilepsia (1998), 39(2), 183-187
CODEN: EPILAK; ISSN: 0013-9580
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In order to determine whether the toxicity that occurs in some patients when lamotrigine (LTG) is added to carbamazepine (CBZ) is the result of either a pharmacokinetic or a pharmacodynamic interaction, escalating LTG doses were added to ongoing CBZ treatment in 47 patients. All patients had blood samples collected for drug concentration measurement, including the epoxide metabolite of CBZ, before starting LTG treatment and after stabilizing at each dose escalation. Patients also were examined for signs of toxicity. After LTG was introduced, nine patients demonstrated clin. signs of CNS toxicity, mainly diplopia and dizziness. There was no significant ($p = 0.05$) change in the serum concns. of either CBZ or its epoxide metabolite when LTG was added either to the group as a whole or to the nine patients who experienced adverse CNS effects. LTG serum concns. also were below the level at which the common signs of LTG toxicity, such as nausea, vomiting, or unsteadiness, are more likely to occur. In seven of the nine patients who exhibited CNS toxicity, CBZ serum concns. were >8 mg/L on LTG introduction. Toxicity is more likely to occur when LTG is added to CBZ if the initial CBZ level is high, typically >8 mg/L. This appears to be the result of a pharmacodynamic interaction. A reduction of CBZ dose usually resolves the toxicity, allowing the LTG dose to be escalated to maximal effect. It is not usually necessary to stop either drug.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 43 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:638497 HCAPLUS
DOCUMENT NUMBER: 125:315860
TITLE: Lamotrigine monotherapy: An overview
AUTHOR(S): Brodie, M. J.
CORPORATE SOURCE: WESTERN INFIRMARY, UNIVERSITY DEPARTMENT MEDICINE AND THERAPEUTICS, Glasgow, UK
SOURCE: International Congress and Symposium Series - Royal Society of Medicine (1996), 214(Lamotrigine--A

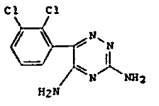
Brighter Future), 43-49
CODEN: RMISDU; ISSN: 0142-2367
PUBLISHER: Royal Society of Medicine Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with .apprx.5 refs. In a pooled population of 784 patients with newly-diagnosed epilepsy participating in comparative monotherapy trials, 443 were randomized to lamotrigine, 246 to carbamazepine and 95 to phenytoin. Overall, fewer patients were withdrawn due to adverse events on lamotrigine than with the older drugs (lamotrigine 9.5%, carbamazepine 19.1%, phenytoin 18.9%). Central nervous system (CNS) problems resulting in withdrawal, in particular, were infrequent with lamotrigine (lamotrigine 2.5%, carbamazepine 7.7%, phenytoin 7.4%). Withdrawal due to rash occurred in 6.1% of patients on lamotrigine, 8.9% on carbamazepine and 5.3% on phenytoin. The rash rate leading to withdrawal with lamotrigine appeared to relate to the initiation dose (100 mg, 11.8%; 50 mg, 9.2%; 25 mg, 2.2%). It is sometimes appropriate to substitute lamotrigine monotherapy for other antiepileptic drug treatments. Schedules for substituting lamotrigine in patients established on phenytoin, carbamazepine or sodium valproate are outlined. In the comparative monotherapy trials, the most popular lamotrigine doses were 150-200 mg daily. In studies in which concomitant antiepileptic drugs (AEDs) were withdrawn to achieve lamotrigine monotherapy, some patients took as much as 700 mg lamotrigine daily. Clin. experience to date does not suggest the existence of a relationship between the plasma lamotrigine concentration and its efficacy or toxicity. Data and case reports from a prospective study in Glasgow relating lamotrigine dosage and concentration to seizure control and the emergence of side effects are presented.

L16 ANSWER 44 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:94551 HCAPLUS
DOCUMENT NUMBER: 124:194132
TITLE: The effects of anticonvulsants on 4-aminopyridine-induced bursting: in vitro studies on rat peripheral nerve and dorsal roots
AUTHOR(S): Lees, G.
CORPORATE SOURCE: Dep. Academic Anaesthetics, Imperial College Medicine, London, W2 1NY, UK
SOURCE: British Journal of Pharmacology (1996), 117(3), 573-9
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Aminopyridines have been used as beneficial symptomatic treatments in a variety of neurol. conditions including multiple sclerosis but have been associated with considerable toxicity in the form of abdominal pain, paraesthesias and (rarely) convulsions. Extracellular and intracellular recording was used to characterize action potentials in rat sciatic nerves and dorsal roots and the effects of 4-aminopyridine (4-AP). In sciatic nerve trunks, 1 mM 4-AP produced pronounced after potentials at room temperature secondary to regenerative firing in affected axons (5-10 spikes per stimulus). At physiol. temps., after potentials (2-3 spikes) were greatly attenuated in peripheral axons. 4-AP evoked more pronounced and prolonged after discharges in isolated dorsal roots at 37°C (3-5.5 mV and 80-100 ms succeeded by a smaller inhibitory/depolarizing voltage shift) which were used to assess the effects of anticonvulsants. Phenytoin, carbamazepine and lamotrigine dose-dependently reduced the area of 4-AP-induced after potentials at 100 and 320 μM but the amplitude of

compound action potentials (evoked at 0.5 Hz) was depressed in parallel. The tonic block of sensory action potentials by all three drugs (at 320 μM) was enhanced by high frequency stimulation (5-500 Hz). The lack of selectivity of these frequency-dependent Na+ channel blockers for burst firing, compared to low-frequency spikes, is discussed in contrast to their effects on 4-AP-induced seizures and paroxysmal activity in CNS tissue (which is associated with large and sustained depolarizing plateau potentials). In conclusion, these in vitro results confirm the marked sensitivity of sensory axons to 4-AP (the presumptive basis for paraesthesias). Burst firing was not preferentially impaired at relatively high concns. suggesting that anticonvulsants will not overcome the toxic peripheral actions of 4-AP in neurol. patients.

L16 ANSWER 45 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:531450 HCAPLUS
DOCUMENT NUMBER: 119:131450
TITLE: Studies on the mechanism of action of the novel anticonvulsant lamotrigine (Lamictal) using primary neuroglial cultures from rat cortex
AUTHOR(S): Lees, George; Leach, Michael J.
CORPORATE SOURCE: Dep. Pharmacol., Wellcome Res. Lab., Beckenham/Kent, BR3 3BS, UK
SOURCE: Brain Research (1993), 612(1-2), 190-9
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Whole cell and perforated patch clamp expts. were conducted on cultured cortical rat neurons (7-21 days in vitro) in order to determine the effects of the anticonvulsant and glutamate release inhibitor lamotrigine (10-100 μM), on CNS receptors and ion channels. The compound inhibited, indiscriminately, both excitatory and inhibitory synaptic events which occurred spontaneously in cultured neural circuits. The drug did not mimic diazepam as a pos. modulator of GABAA currents. In the presence of tetrodotoxin, voltage-gated potassium currents and composite currents evoked by L-glutamate were not significantly modulated even at the highest dose. Unitary, fast, presumptive-sodium spikes, evoked at low frequencies, were not blocked significantly by lamotrigine. In contrast, burst firing induced by pulsed application of L-glutamate or potassium ions was markedly depressed at 10 μM. Presumptive calcium currents were inhibited by lamotrigine at 100 μM. It is proposed that the drug inhibits epileptiform burst firing preferentially by state/activity dependent interactions with voltage and gated cation channels. Potential mechanisms for inhibition of glutamate release are discussed.

L16 ANSWER 46 OF 46 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:102360 HCAPLUS
DOCUMENT NUMBER: 104:102360
TITLE: Lamotrigine (BW430C), a potential anticonvulsant. Effects on the central nervous system in comparison with phenytoin and diazepam
AUTHOR(S): Cohen, A. F.; Ashby, L.; Crowley, D.; Land, G.; Peck, A. W.; Miller, A. A.
CORPORATE SOURCE: Wellcome Res. Lab., Beckenham/Kent, UK
SOURCE: British Journal of Clinical Pharmacology (1985), 20(6), 619-29
CODEN: BCPHBM; ISSN: 0306-5251
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Healthy male volunteers received phenytoin [57-41-0] 0.5 and 1 g, lamotrigine (I) [84057-84-1] (a new anticonvulsant) 120 and 240 mg, diazepam [439-14-5] 10 mg and placebo orally in a double-blind, cross-over, randomized trail. Maximum drug concns. at 4 h, measured in plasma were 11.5 μg/mL for phenytoin and 2.7 μg/mL for lamotrigine. These levels were in the therapeutic range for phenytoin and the putative therapeutic range for lamotrigine. Side effects after diazepam (mainly sedation) and phenytoin (mainly unsteadiness) differed markedly from lamotrigine which produced no important side effects. Subjective effects as measured by visual analog scales were caused by phenytoin and diazepam but not by lamotrigine. Diazepam impaired eye movements, adaptive tracking and body sway. Phenytoin impaired adaptive tracking, increased body sway and impaired smooth pursuit eye movement. Lamotrigine produced only a possible slight increase in body sway. There were significant correlations between performance and saliva levels of phenytoin and diazepam. The tests used were suitable for monitoring central nervous system (CNS) effects of anticonvulsants and lamotrigine possibly could have a more favorable CNS side effect than phenytoin.

=> d his

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L3 128 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 16:56:47 ON 04 APR 2007
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L5 0 S E3/RN
L6 1 S E3

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L7 0 S L6

FILE 'HCAPLUS' ENTERED AT 17:00:04 ON 04 APR 2007
E LAMOTRIGINE+ALL/CT
S LAMOTRIGINE/CN

FILE 'REGISTRY' ENTERED AT 17:00:26 ON 04 APR 2007
L8 1 S LAMOTRIGINE/CN

FILE 'HCAPLUS' ENTERED AT 17:00:27 ON 04 APR 2007
L9 1265 S L8

L10 27 S "3,5-DIAMINO-6-(2,3-DICHLOROPHENYL)-1,2,4-TRIAZINE"

FILE 'REGISTRY' ENTERED AT 17:02:26 ON 04 APR 2007
L11 1 S 84057-84-1/RN

FILE 'HCAPLUS' ENTERED AT 17:02:48 ON 04 APR 2007
L12 1265 S L11
L13 111187 S L10 OR L12 AND PARTICLE OR GRANULE
L14 0 S L12 (N) PARTICLE
L15 0 S L12 (W) PARTICLE
L16 46 S L12 AND CNS

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             8 SAMBURSKI,G?/AU
L17         91 ARONHIME,J?/AU OR SAMBURSKI,G?/AU

=> s aronhime,j?/au and samburski,g?/au
            86 ARONHIME,J?/AU
             8 SAMBURSKI,G?/AU
L18          3 ARONHIME,J?/AU AND SAMBURSKI,G?/AU

=> d l18 1-3 ibib abs

L18  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:259910  HCAPLUS
DOCUMENT NUMBER:          146:281059
TITLE:                    Solid particulate tadalafil having a bimodal particle
                          size distribution
INVENTOR(S):              Aronhime, Judith; Samburski, Guy;
                          Ovadya, Yhoshoa
PATENT ASSIGNEE(S):       Teva Pharmaceutical Industries Ltd., Israel; Teva
                          Pharmaceuticals USA, Inc.
SOURCE:                   PCT Int. Appl., 19pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    -------------------     --------
     WO 2007027612         A2    20070308    WO 2006-US33541         20060829
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
             KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
             MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
             RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                    US 2005-712589P     P  20050829
AB   Provided is a solid particulate tadalafil having a bimodal particle size
     distribution.  The solid particulate tadalafil is useful for the manufacture of
     a medicament for the treatment of sexual dysfunction.  Thus, 2 g of a
     solid particulate tadalafil having a bimodal particle size distribution
     were prepared by combining 0.38 g of large particle size tadalafil and 1.62
     g of small particle size tadalafil.  Calcn. of the amount of large particle
     size particulate tadalafil was presented.

L18  ANSWER 2 OF 3  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2006:543943  HCAPLUS
DOCUMENT NUMBER:          145:45919
TITLE:                    Process for the preparation of ezetimibe polymorphic
                          crystalline forms
INVENTOR(S):              Aronhime, Judith; Koltai, Tamas;
                          Samburski, Guy; Lehrman, Ori; Izsak, Reuven
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PATENT ASSIGNEE(S):       Teva Pharmaceutical Industries Ltd., Israel; Teva
                          Pharmaceuticals Usa, Inc.
SOURCE:                   PCT Int. Appl., 54 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    -------------------     --------
     WO 2006060808         A1    20060608    WO 2005-US44065         20051205
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
             MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
             SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
             VN, YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
     US 2006160785         A1    20060720    US 2005-295141          20051205
PRIORITY APPLN. INFO.:                    US 2004-632543P     P  20041203
                                          US 2005-649139P     P  20050203
                                          US 2005-668571P     P  20050406
                                          US 2005-687316P     P  20050606
                                          US 2005-712781P     P  20050830
                                          US 2005-717275P     P  20050914
AB   Processes are described for preparing polymorphic crystalline forms of
ezetimibe,
     such as ezetimibe Form A or Form B, for example, by precipitating ezetimibe
from
     selected solvents.  Some forms may be transformed into different forms at
     elevated temps., or under various humidity conditions, or by
     micronization.
REFERENCE COUNT:          8     THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18  ANSWER 3 OF 3  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2003:875073  HCAPLUS
DOCUMENT NUMBER:          139:354488
TITLE:                    Pharmaceutical composition containing lamotrigine
                          particles of defined morphology
INVENTOR(S):              Aronhime, Judith; Samburski, Guy
PATENT ASSIGNEE(S):       Teva Pharmaceutical Industries Ltd., Israel; Teva
                          Pharmaceuticals USA, Inc.
SOURCE:                   PCT Int. Appl., 24 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    -------------------     --------
     WO 2003090693         A2    20031106    WO 2003-US13002         20030423
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WO 2003090693	A3	20040108			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2483103	A1	20031106	CA 2003-2483103		20030423
AU 2003234240	A1	20031110	AU 2003-234240		20030423
EP 1496864	A2	20050119	EP 2003-728552		20030423
EP 1496864	B1	20070321			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
US 2005238724	A1	20051027	US 2004-511987		20041021
PRIORITY APPLN. INFO.:			US 2002-374923P	P	20020423
			WO 2003-US13002	W	20030423

AB The present invention provides a pharmaceutical composition comprising a plurality of lamotrigine particles having a sp. surface area of from about two to about three and a half meters per g. Pharmaceutical compns. falling within the surface area criteria for the lamotrigine particles include those having a particle diameter equal to or less than about 100 μm, preferably about 50 μm, and most preferably 10 μm. The pharmaceutical composition can be formulated into a wide variety of dosage forms for treatment of seizures.